=> fil reg
FILE 'REGISTRY' ENTERED AT 08:49:32 ON 30 JAN 2004
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 28 JAN 2004 HIGHEST RN 642928-00-5
DICTIONARY FILE UPDATES: 28 JAN 2004 HIGHEST RN 642928-00-5

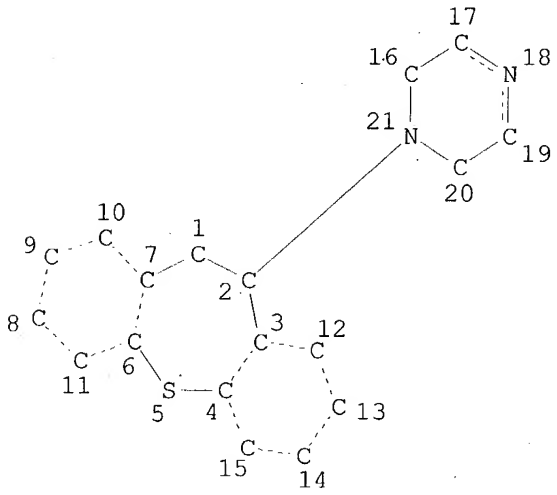
TSCA INFORMATION NOW CURRENT THROUGH JULY 14, 2003

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more information enter HELP PROP at an arrow prompt in the file or refer to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

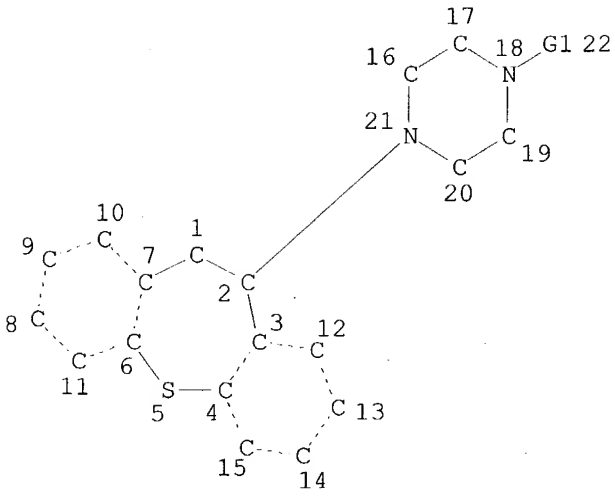
=> d sta que l9
L1 STR



NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

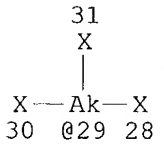
GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 21

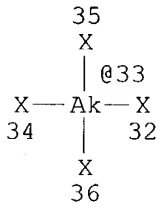
STEREO ATTRIBUTES: NONE
L3 1769 SEA FILE=REGISTRY SSS FUL L1
L4 STR

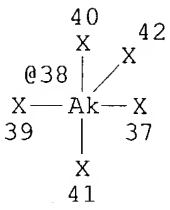


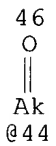
Ak—X
@23 24

X—Ak—X
27 @26 25









VAR G1=AK/23/26/29/33/38/44
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CONNECT IS M1 RC AT 9
CONNECT IS M1 RC AT 10
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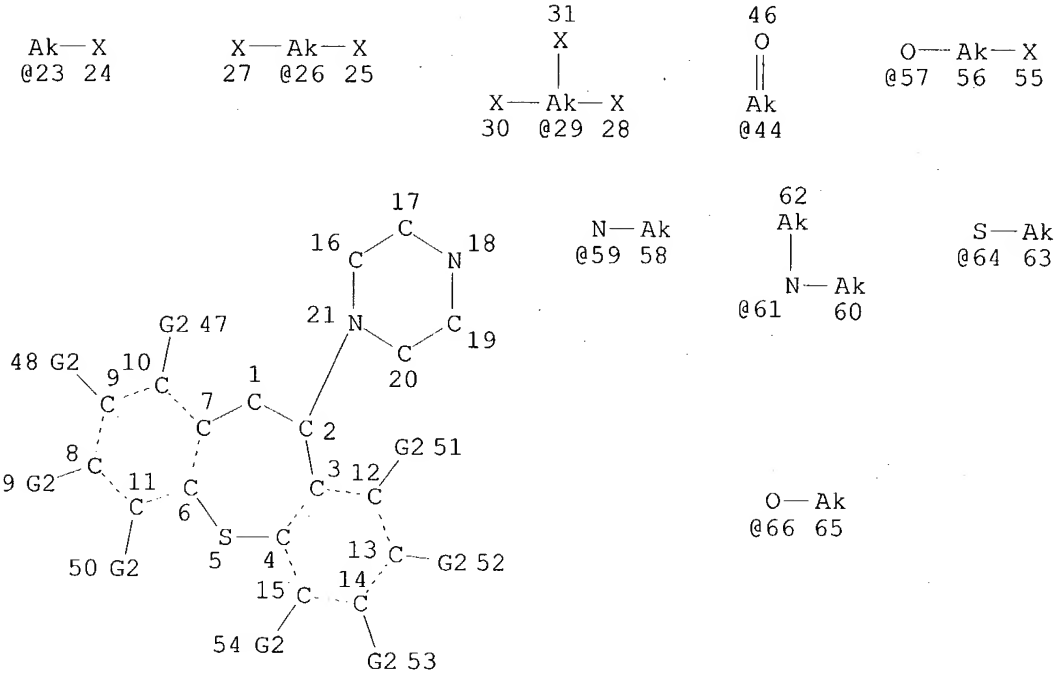
CONNECT IS M1 RC AT 12
CONNECT IS M1 RC AT 13
CONNECT IS M1 RC AT 14
CONNECT IS M1 RC AT 15
CONNECT IS M1 RC AT 38
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RSPEC I
NUMBER OF NODES IS 44

STEREO ATTRIBUTES: NONE
L6 561 SEA FILE=REGISTRY SUB=L3 CSS FUL L4
L7 STR



VAR G2=H/X/AK/66/64/23/26/29/57/NO2/CN/44/NH2/59/61
NODE ATTRIBUTES:
CONNECT IS M1 RC AT 18
CONNECT IS M1 RC AT 29
CONNECT IS M1 RC AT 56
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RSPEC I
NUMBER OF NODES IS 52

STEREO ATTRIBUTES: NONE
L9 457 SEA FILE=REGISTRY SUB=L6 CSS FUL L7

100.0% PROCESSED 561 ITERATIONS 457 ANSWERS
SEARCH TIME: 00.00.01

=> d his

(FILE 'HOME' ENTERED AT 08:04:17 ON 30 JAN 2004)
DEL HIS

FILE 'REGISTRY' ENTERED AT 08:05:18 ON 30 JAN 2004
L1 STR
L2 50 S L1
L3 1769 S L1 FUL
SAV TEMP L3 LE061/A
L4 STR L1
L5 25 S L4 CSS SAM SUB=L3
L6 561 S L4 CSS FUL SUB=L3
SAV TEMP L6 LE061A/A
L7 STR L4
L8 19 S L7 CSS SAM SUB=L6

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L9          457 S L7 CSS FUL SUB=L6
                SAV TEMP L9 LE061B/A

     FILE 'HCAPLUS' ENTERED AT 08:20:19 ON 30 JAN 2004
L10         618 S L9
L11       13257 S CMV OR ?CYTOMEGALOVIR?
                E CYTOMEGALOVIR/CT
                E E4+ALL
L12        2971 S E7
L13        5744 S E6+NT
                E CYTOMEG/CT
                E E6+ALL
L14           2 S L10 AND L11-L13
                E SCHALL T/AU
L15         128 S E3-E10
                E PENFOLD M/AU
L16          17 S E4-E6
                E CHEMOCENTR/PA,CS
L17          33 S E5-E14
                E CHEMO CENTR/PA,CS
L18           2 S L10 AND L15-L17
L19           1 S US20020182594/PN OR (WO2002-US3229 OR US2001-266094#)/AP,PRN
L20           3 S L14,L18,L19
L21           3 S L20 AND L10-L20
                SEL HIT RN

     FILE 'REGISTRY' ENTERED AT 08:24:11 ON 30 JAN 2004
L22           4 S E1-E4

     FILE 'REGISTRY' ENTERED AT 08:24:33 ON 30 JAN 2004

     FILE 'MEDLINE' ENTERED AT 08:24:56 ON 30 JAN 2004
L23         356 S L9
L24         989 S OCTOCLOTHEPIN? OR CLOTEPIN? OR CLOTHEPIN? OR CLOROTHEPIN? OR
L25         989 S L23,L24
L26       28347 S L11
                E CYTOMEGALOVIR/CT
                E E6+ALL
L27       11117 S E9+NT
                E CYTOMEGALOVIR/CT
                E E9+ALL
L28       14342 S E5+NT
                E CYTOMEGALOVIR/CT
                E E77+ALL
L29          22 S E10+NT
                E CYTOMEGALOVIRUS/CT
                E E82+ALL
L30        1546 S E2+NT
L31         351 S E4+NT
L32           0 S L25 AND L26-L31
                E SCHALL T/AU
L33          89 S E3-E7
                E PENFOLD M/AU
L34          12 S E3-E5,E8,E9
L35           0 S L25 AND L33,L34
L36          10 S L26-L31 AND L33,L34

     FILE 'BIOSIS' ENTERED AT 08:31:11 ON 30 JAN 2004
L37        1228 S L25
L38       31590 S L11
L39       82214 S HERPESVIRIDAE+NT/BC
                E 02220/BC
                E 02162/BC
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                E CYTOMEGA/BC
                E HERP/BC
L40           0 S L37 AND L38,L39
                E SCHALL T/AU
L41         146 S E3-E9
                E PENFOLD M/AU
L42          13 S E4-E7
L43           0 S L37 AND L41,L42
L44          16 S L38,L39 AND L41,L42

     FILE 'MEDLINE, BIOSIS' ENTERED AT 08:49:21 ON 30 JAN 2004
L45          16 DUP REM L36 L44 (10 DUPLICATES REMOVED)

     FILE 'REGISTRY' ENTERED AT 08:49:32 ON 30 JAN 2004

=> d ide can tot l22

L22  ANSWER 1 OF 4  REGISTRY  COPYRIGHT 2004 ACS on STN
RN   74611-28-2  REGISTRY
CN   Piperazine, 1-[10,11-dihydro-8-(methylthio)dibenzo[b,f]thiepin-10-yl]-4-
     methyl-, monomethanesulfonate (9CI)  (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN   Dibenzo[b,f]thiepin, piperazine deriv.
MF   C20 H24 N2 S2 . C H4 O3 S
LC   STN Files:   BEILSTEIN*, CA, CAPLUS, USPATFULL
         (*File contains numerically searchable property data)

     CM   1

     CRN  20229-30-5
     CMF  C20 H24 N2 S2
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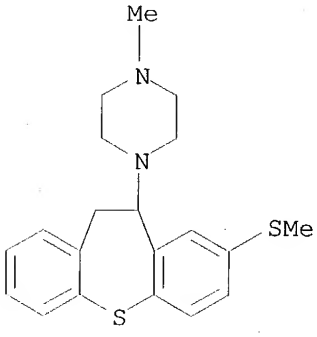


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     CM   2

     CRN  75-75-2
     CMF  C H4 O3 S
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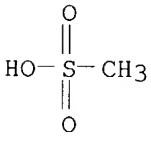


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              4 REFERENCES IN FILE CA (1907 TO DATE)
              4 REFERENCES IN FILE CAPLUS (1907 TO DATE)
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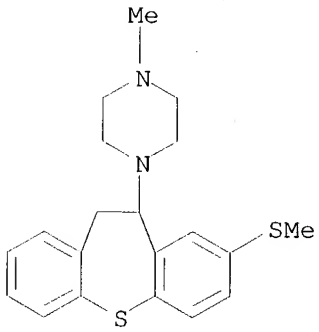
REFERENCE 1: 138:350028

REFERENCE 2: 136:210544

REFERENCE 3: 110:108076

REFERENCE 4: 93:95239

L22 ANSWER 2 OF 4 REGISTRY COPYRIGHT 2004 ACS on STN
RN **20229-30-5** REGISTRY
CN Piperazine, 1-[10,11-dihydro-8-(methylthio)dibenzo[b,f]thiepin-10-yl]-4-methyl- (8CI, 9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Dibenzo[b,f]thiepin, piperazine deriv.
OTHER NAMES:
CN Methiotepin
CN Methiothepin
CN Methiothepine
CN Metitepine
CN Ro 8-6837
DR 101395-30-6
MF C20 H24 N2 S2
CI COM
LC STN Files: AGRICOLA, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAPLUS, CASREACT, CHEMCATS, DDFU, DRUGU, EMBASE, IPA, MEDLINE, MRCK*, PROMT, RTECS*, SYNTHLINE, TOXCENTER, USAN, USPATFULL, VETU
(*File contains numerically searchable property data)
Other Sources: WHO



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

328 REFERENCES IN FILE CA (1907 TO DATE)
3 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
328 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 140:53411

REFERENCE 2: 140:38959

REFERENCE 3: 139:376851

REFERENCE 4: 139:191441

REFERENCE 5: 139:111697

REFERENCE 6: 139:95704

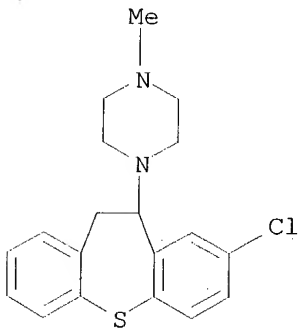
REFERENCE 7: 139:95476

REFERENCE 8: 139:66336

REFERENCE 9: 138:150503

REFERENCE 10: 138:130917

L22 ANSWER 3 OF 4 REGISTRY COPYRIGHT 2004 ACS on STN
RN **13448-22-1** REGISTRY
CN Piperazine, 1-(8-chloro-10,11-dihydrodibenzo[b,f]thiepin-10-yl)-4-methyl- (8CI, 9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Dibenzo[b,f]thiepin, piperazine deriv.
OTHER NAMES:
CN (±)-Clothepin
CN (±)-Octoclothepin
CN Chlorothepin
CN Clorotepine
CN Clotepin
CN Clothepin
CN Octoclothepin
CN Octoclothepine
DR 41931-02-6
MF C19 H21 Cl N2 S
CI COM
LC STN Files: AGRICOLA, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CAPLUS, CASREACT, DDFU, DRUGU, EMBASE, IPA, MEDLINE, PHAR, PROMT, RTECS*, TOXCENTER, USAN, USPATFULL
(*File contains numerically searchable property data)
Other Sources: WHO



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

103 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
103 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 139:62616

REFERENCE 2: 137:103378

REFERENCE 3: 136:226769

REFERENCE 4: 136:210544

REFERENCE 5: 136:112520

REFERENCE 6: 134:126129

REFERENCE 7: 132:288780

REFERENCE 8: 128:110756

REFERENCE 9: 125:50947

REFERENCE 10: 120:289951

L22 ANSWER 4 OF 4 REGISTRY COPYRIGHT 2004 ACS on STN
RN **4789-68-8** REGISTRY
CN Piperazine, 1-(8-chloro-10,11-dihydrodibenzo[b,f]thiepin-10-yl)-4-methyl-, (2Z)-2-butenedioate (1:1) (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Dibenzo[b,f]thiepin, piperazine deriv.
CN Piperazine, 1-(8-chloro-10,11-dihydrodibenzo[b,f]thiepin-10-yl)-4-methyl-, (Z)-2-butenedioate (1:1)
CN Piperazine, 1-(8-chloro-10,11-dihydrodibenzo[b,f]thiepin-10-yl)-4-methyl-, maleate (1:1) (8CI)
OTHER NAMES:
CN Octoclothepin maleate
FS STEREOSEARCH
DR 41931-03-7
MF C19 H21 Cl N2 S . C4 H4 O4
LC STN Files: BEILSTEIN*, CA, CAOLD, CAPLUS, CHEMCATS, RTECS*, TOXCENTER, USPATFULL
(*File contains numerically searchable property data)

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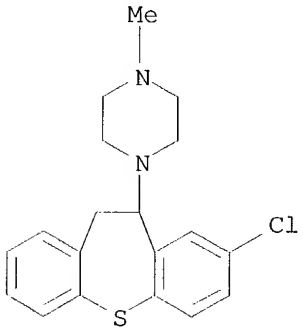
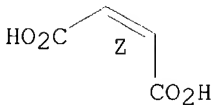
CRN 13448-22-1
CMF C19 H21 Cl N2 S



CM 2

CRN 110-16-7
CMF C4 H4 O4

Double bond geometry as shown.



17 REFERENCES IN FILE CA (1907 TO DATE)
17 REFERENCES IN FILE CAPLUS (1907 TO DATE)
1 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 138:350028

REFERENCE 2: 136:210544

REFERENCE 3: 135:335153

REFERENCE 4: 90:33708

REFERENCE 5: 89:123059

REFERENCE 6: 88:182362

REFERENCE 7: 88:288

REFERENCE 8: 80:70836

REFERENCE 9: 80:59966

REFERENCE 10: 79:92282

=> fil hcaplus
FILE 'HCAPLUS' ENTERED AT 08:49:55 ON 30 JAN 2004
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

FILE COVERS 1907 - 30 Jan 2004 VOL 140 ISS 6
FILE LAST UPDATED: 29 Jan 2004 (20040129/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> d all hitstr tot l21

L21 ANSWER 1 OF 3 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:615791 HCAPLUS
DN 137:151988
ED Entered STN: 16 Aug 2002
TI Chemomagnetic retrieval of **CMV** and **CMV** infected cells

and apparatus
IN **Schall, Thomas J.; Penfold, Mark E. T.**
PA **Chemocentryx, Inc., USA**
SO PCT Int. Appl., 41 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C12N
CC 9-1 (Biochemical Methods)
Section cross-reference(s): 1, 3, 10, 14, 63
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002062956	A2	20020815	WO 2002-US3229	20020201 <--
	WO 2002062956	A3	20030227		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

	US 2002182594	A1	20021205	US 2002-61944	20020201 <--
PRAI	US 2001-266094P	P	20010202 <--		

OS MARPAT 137:151988
AB Methods and apparatus are provided herein for collecting **CMV** and/or **CMV** infected cells from a host infected with **CMV**. Such methods and apparatus have utility in tracking the dissemination or infection of the host, use as an in vivo or ex vivo collection mechanism to measure mutation rates and selective pressures after in vivo passage, and in therapeutic treatments in which **CMV** and/or **CMV** infected cells are removed from a host.
ST chemomagnetic retrieval **cytomegalovirus** infected cell; app collection **cytomegalovirus** infected cell; **cytomegalovirus** infected cell removal app
IT Proteins
RL: BSU (Biological study, unclassified); REM (Removal or disposal); BIOL (Biological study); PROC (Process)
(US28, apparatus with ligand binding to **cytomegalovirus**; chemomagnetic retrieval of **CMV** and **CMV** infected cells and apparatus)
IT Gelatins, biological studies
Polyesters, biological studies
Polyurethanes, biological studies
RL: BUU (Biological use, unclassified); DEV (Device component use); TEM (Technical or engineered material use); BIOL (Biological study); USES (Uses)
(as absorptive material in implant; chemomagnetic retrieval of **CMV** and **CMV** infected cells and apparatus)
IT Particles
(beads, with compound binding to **cytomegalovirus**; chemomagnetic retrieval of **CMV** and **CMV** infected cells and apparatus)
IT Magnetic materials
(chemo-; chemomagnetic retrieval of **CMV** and **CMV** infected cells and apparatus)
IT Absorbents
Apparatus
Blood
Cell
Cytomegalovirus

Mammalia
Medical equipment
Pumps
Sampling apparatus
(chemomagnetic retrieval of **CMV** and **CMV** infected cells and apparatus)

IT Skin
(collection apparatus with patch for application to; chemomagnetic retrieval of **CMV** and **CMV** infected cells and apparatus)

IT Drug resistance
(determination of mutation confering; chemomagnetic retrieval of **CMV** and **CMV** infected cells and apparatus)

IT Genetic selection
(determination of pressures for; chemomagnetic retrieval of **CMV** and **CMV** infected cells and apparatus)

IT Mutation
(determination of rates of; chemomagnetic retrieval of **CMV** and **CMV** infected cells and apparatus)

IT Circulation
(extracorporeal; chemomagnetic retrieval of **CMV** and **CMV** infected cells and apparatus)

IT Ligands
RL: BUU (Biological use, unclassified); DEV (Device component use); TEM (Technical or engineered material use); BIOL (Biological study); USES (Uses)
(for **cytomegalovirus**; chemomagnetic retrieval of **CMV** and **CMV** infected cells and apparatus)

IT Prosthetic materials and Prosthetics
(implants, with ligand binding to **cytomegalovirus**; chemomagnetic retrieval of **CMV** and **CMV** infected cells and apparatus)

IT Medical goods
(sponges; chemomagnetic retrieval of **CMV** and **CMV** infected cells and apparatus)

IT Infection
(viral; chemomagnetic retrieval of **CMV** and **CMV** infected cells and apparatus)

IT Colloids
Microspheres
Nanoparticles
(with compound binding to **cytomegalovirus**; chemomagnetic retrieval of **CMV** and **CMV** infected cells and apparatus)

IT Collecting apparatus
(with ligand binding to **cytomegalovirus**; chemomagnetic retrieval of **CMV** and **CMV** infected cells and apparatus)

L21 ANSWER 2 OF 3 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:172238 HCAPLUS
DN 136:226769
ED Entered STN: 08 Mar 2002
TI US28 and homolog expression by **cytomegaloviruses** and its interaction with chemokines as a basis to prevent **cytomegalovirus** infection and dissemination
IN **Schall, Thomas J.; Penfold, Mark**
PA **Chemocentryx, Inc., USA**
SO PCT Int. Appl., 95 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM G01N033-569
ICS A61P031-12; A61K039-395; A61K048-00; C07K014-00; C12N015-00; C12N005-00
CC 1-5 (Pharmacology)

Section cross-reference(s): 3, 10, 15

FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002018954	A2	20020307	WO 2001-US27392	20010830
	WO 2002018954	C2	20030327		
	WO 2002018954	A3	20030724		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	AU 2001088682	A5	20020313	AU 2001-88682	20010830
	US 2002127544	A1	20020912	US 2001-944163	20010830
	US 2003175681	A1	20030918	US 2001-944049	20010830
	EP 1350113	A2	20031008	EP 2001-968433	20010830
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
PRAI	US 2000-229365P	P	20000830		
	US 2000-228974P	P	20000830		
	US 2000-229191P	P	20000830		
	WO 2001-US27392	W	20010830		

AB The invention provides methods and compns. for inhibiting **cytomegalovirus** (**CMV**) infection and dissemination in an animal, as well as in vitro and in vivo assay systems for identifying such compns. US28 is expressed by human **cytomegalovirus** as a viorion mol. capable of interacting with fractalkine with high affinity. Rhesus monkey **cytomegalovirus** expresses at least 5 homologs, with similar chemokine binding activity. **CMV** dissemination in infected hosts can be inhibited by administration of an inhibitor (e.g., octoclotheptin) of the US28-receptor interaction. Thus, this invention provides screening methods for agents that reduce **CMV** dissemination in an animal, and treatment of **CMV** infection.

ST US28 homolog gene sequence chemokine interaction **cytomegalovirus** ; antiviral screening **cytomegalovirus** US28 chemokine interaction

IT Chemokines
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(C-C; US28 and homolog expression by **cytomegaloviruses** and its interaction with chemokines as a basis to prevent **cytomegalovirus** infection and dissemination)

IT Chemokines
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(C-X-C; US28 and homolog expression by **cytomegaloviruses** and its interaction with chemokines as a basis to prevent **cytomegalovirus** infection and dissemination)

IT Antiviral agents
Cercopithecine herpesvirus 8
DNA sequences
Drug screening
Gene therapy
Human herpesvirus 5
Molecular cloning
Protein sequences
Vaccines
cDNA sequences
(US28 and homolog expression by **cytomegaloviruses** and its interaction with chemokines as a basis to prevent **cytomegalovirus** infection and dissemination)

IT Chemokines

Eotaxin
Macrophage inflammatory protein 1α
Macrophage inflammatory protein 1β
Monocyte chemoattractant protein-1
Monocyte chemoattractant protein-2
RANTES (chemokine)
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(US28 and homolog expression by **cytomegaloviruses** and its interaction with chemokines as a basis to prevent **cytomegalovirus** infection and dissemination)

IT Proteins
RL: ANT (Analyte); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(US28; US28 and homolog expression by **cytomegaloviruses** and its interaction with chemokines as a basis to prevent **cytomegalovirus** infection and dissemination)

IT Proteins
RL: ANT (Analyte); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(US33; US28 and homolog expression by **cytomegaloviruses** and its interaction with chemokines as a basis to prevent **cytomegalovirus** infection and dissemination)

IT Proteins
RL: ANT (Analyte); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(US78; US28 and homolog expression by **cytomegaloviruses** and its interaction with chemokines as a basis to prevent **cytomegalovirus** infection and dissemination)

IT Nucleic acid amplification (method)
(determination of viral titer by; US28 and homolog expression by **cytomegaloviruses** and its interaction with chemokines as a basis to prevent **cytomegalovirus** infection and dissemination)

IT Blood analysis
Saliva
Urine analysis
(determination of viral titer in; US28 and homolog expression by **cytomegaloviruses** and its interaction with chemokines as a basis to prevent **cytomegalovirus** infection and dissemination)

IT Chemokines
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(fractalkines; US28 and homolog expression by **cytomegaloviruses** and its interaction with chemokines as a basis to prevent **cytomegalovirus** infection and dissemination)

IT Animal
Primates
(screening for active agents in; US28 and homolog expression by **cytomegaloviruses** and its interaction with chemokines as a basis to prevent **cytomegalovirus** infection and dissemination)

IT Antisense DNA
Ribozymes
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(targeting US28; US28 and homolog expression by **cytomegaloviruses** and its interaction with chemokines as a basis to prevent **cytomegalovirus** infection and dissemination)

IT **13448-22-1**, Octoclothepine
RL: PAC (Pharmacological activity); BIOL (Biological study)
(US28 and homolog expression by **cytomegaloviruses** and its interaction with chemokines as a basis to prevent **cytomegalovirus** infection and dissemination)

IT 403674-88-4 403674-90-8 403674-92-0 403674-94-2 403674-96-4

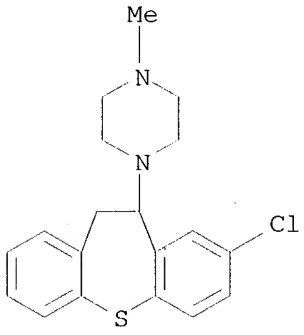
403674-98-6 403675-00-3 403675-02-5 403675-04-7 403675-06-9
403675-08-1 403675-10-5 403675-12-7
RL: ANT (Analyte); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(amino acid sequence; US28 and homolog expression by **cytomegaloviruses** and its interaction with chemokines as a basis to prevent **cytomegalovirus** infection and dissemination)

IT 403674-87-3 403674-89-5 403674-91-9 403674-93-1 403674-95-3
403674-97-5 403674-99-7 403675-01-4 403675-03-6 403675-05-8
403675-07-0 403675-09-2 403675-11-6
RL: ANT (Analyte); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(nucleotide sequence; US28 and homolog expression by **cytomegaloviruses** and its interaction with chemokines as a basis to prevent **cytomegalovirus** infection and dissemination)

IT 403679-03-8 403679-04-9 403679-05-0 403679-06-1 403679-07-2
403679-08-3 403679-09-4 403679-10-7 403679-11-8 403679-12-9
403679-13-0 403679-14-1 403679-15-2 403679-16-3 403679-17-4
403679-18-5 403679-19-6 403679-20-9 403679-21-0 403679-22-1
403679-23-2
RL: PRP (Properties)
(unclaimed nucleotide sequence; uS28 and homolog expression by **cytomegaloviruses** and its interaction with chemokines as a basis to prevent **cytomegalovirus** infection and dissemination)

IT **13448-22-1**, Octoclothepine
RL: PAC (Pharmacological activity); BIOL (Biological study)
(US28 and homolog expression by **cytomegaloviruses** and its interaction with chemokines as a basis to prevent **cytomegalovirus** infection and dissemination)

RN 13448-22-1 HCAPLUS
CN Piperazine, 1-(8-chloro-10,11-dihydrodibenzo[b,f]thiepin-10-yl)-4-methyl- (8CI, 9CI) (CA INDEX NAME)



L21 ANSWER 3 OF 3 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:171670 HCAPLUS
DN 136:210544
ED Entered STN: 08 Mar 2002
TI Modulators of US28 chemokine receptors and their use for blocking **cytomegalovirus** dissemination
IN **Schall, Thomas J.**; McMaster, Brian E.; Dairaghi, Daniel J.
PA **Chemocentryx, Inc., USA**
SO PCT Int. Appl., 28 pp.
CODEN: PIXXD2
DT Patent
LA English

IC ICM A61K031-00
CC 1-5 (Pharmacology)
FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002017900	A2	20020307	WO 2001-US27363	20010830
	WO 2002017900	A3	20030626		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

	AU 2001087043	A5	20020313	AU 2001-87043	20010830
	US 2002127544	A1	20020912	US 2001-944163	20010830
PRAI	US 2000-228974P	P	20000830		
	US 2000-229191P	P	20000830		
	US 2000-229365P	P	20000830		
	WO 2001-US27363	W	20010830		

OS MARPAT 136:210544

AB Assays, compns. and methods of treatment are provided for modulating the binding of chemokines to US28 chemokine receptors on the surface of cells. In one aspect, the present invention provides an assay for identifying a compound useful for blocking **cytomegalovirus** (**CMV**) dissemination in a host by determining whether the compound inhibits the binding of a chemokine to US28 or a US28 fragment. Typically, the assay will be run as a competitive binding assay using a labeled chemokine. A variety of chemokines are known to bind to US28 and are useful in this aspect of the invention. Preferably, the chemokine is fractalkine and the assay is a radioligand binding assay. In another aspect, the present invention provides methods for blocking **CMV** dissemination in a host by administering to the host an effective amount of a compound which blocks the binding of a chemokine to US28. Preferably, the compound is one which was identified using an assay of the present invention. In yet another aspect, the present invention provides pharmaceutical compns. for the treatment of **CMV** comprising compds. identified in the present assays.

ST US28 chemokine receptor modulator **cytomegalovirus** dissemination

IT Chemokine receptors
RL: BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(US28; modulators of US28 chemokine receptors and their use for blocking **cytomegalovirus** dissemination)

IT Drug delivery systems
(carriers; modulators of US28 chemokine receptors and their use for blocking **cytomegalovirus** dissemination)

IT Cell migration
(decrease in **cytomegalovirus**-infected cells; modulators of US28 chemokine receptors and their use for blocking **cytomegalovirus** dissemination)

IT Indicators
(for fractalkine; modulators of US28 chemokine receptors and their use for blocking **cytomegalovirus** dissemination)

IT Chemokines
RL: BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(fractalkines; modulators of US28 chemokine receptors and their use for blocking **cytomegalovirus** dissemination)

IT Antiviral agents

Cytomegalovirus
Drug screening
(modulators of US28 chemokine receptors and their use for blocking **cytomegalovirus** dissemination)

IT Chemokines
Macrophage inflammatory protein 1α
Macrophage inflammatory protein 1β
Monocyte chemoattractant protein-1
RANTES (chemokine)
RL: BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(modulators of US28 chemokine receptors and their use for blocking **cytomegalovirus** dissemination)

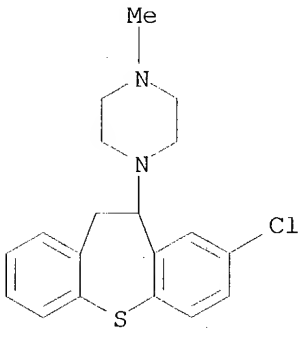
IT **4789-68-8**, Octoclothepin maleate **13448-22-1**, Octoclothepin **20229-30-5**, Methiothepin **74611-28-2**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(modulators of US28 chemokine receptors and their use for blocking **cytomegalovirus** dissemination)

IT **4789-68-8**, Octoclothepin maleate **13448-22-1**, Octoclothepin **20229-30-5**, Methiothepin **74611-28-2**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(modulators of US28 chemokine receptors and their use for blocking **cytomegalovirus** dissemination)

RN 4789-68-8 HCAPLUS
CN Piperazine, 1-(8-chloro-10,11-dihydrodibenzo[b,f]thiepin-10-yl)-4-methyl-, (2Z)-2-butenedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

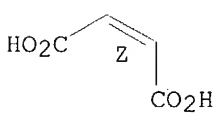
CRN 13448-22-1
CMF C19 H21 Cl N2 S



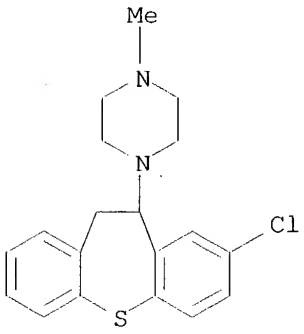
CM 2

CRN 110-16-7
CMF C4 H4 O4

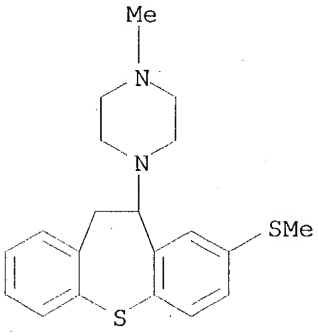
Double bond geometry as shown.



RN 13448-22-1 HCAPLUS
CN Piperazine, 1-(8-chloro-10,11-dihydrodibenzo[b,f]thiepin-10-yl)-4-methyl- (8CI, 9CI) (CA INDEX NAME)



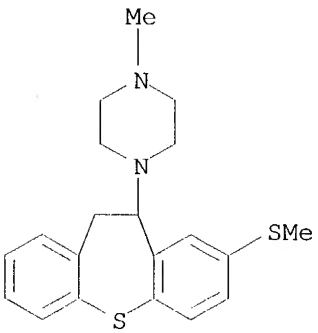
RN 20229-30-5 HCAPLUS
CN Piperazine, 1-[10,11-dihydro-8-(methylthio)dibenzo[b,f]thiepin-10-yl]-4-methyl- (8CI, 9CI) (CA INDEX NAME)



RN 74611-28-2 HCAPLUS
CN Piperazine, 1-[10,11-dihydro-8-(methylthio)dibenzo[b,f]thiepin-10-yl]-4-methyl-, monomethanesulfonate (9CI) (CA INDEX NAME)

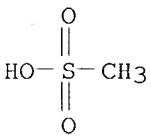
CM 1

CRN 20229-30-5
CMF C20 H24 N2 S2



CM 2

CRN 75-75-2
CMF C H4 O3 S



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FILE 'BIOSIS' ENTERED AT 08:50:44 ON 30 JAN 2004
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L45 ANSWER 1 OF 16 MEDLINE on STN DUPLICATE 1
AN 2003429548 MEDLINE
DN 22850808 PubMed ID: 12970425
TI Characterization of the rhesus **cytomegalovirus** US28 locus.
AU **Penfold M E T**; Schmidt T L; Dairaghi D J; Barry P A; **Schall T J**
CS ChemoCentryx, San Carlos, California 94070, USA..
mpenfold@chemocentryx.com
SO JOURNAL OF VIROLOGY, (2003 Oct) 77 (19) 10404-13.
Journal code: 0113724. ISSN: 0022-538X.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200310
ED Entered STN: 20030913
Last Updated on STN: 20031015
Entered Medline: 20031014
AB Human **cytomegalovirus** (**CMV**) US28 (and the related open reading frame [ORF] US27) are G-protein-coupled receptor homologs believed to play a role in viral pathogenesis. In vitro, US28 has been shown to bind and internalize ligands, as well as activate intracellular signaling in response to certain chemokines, and to initiate the migration of smooth muscle cells to chemokine gradients. To assess the role of US28 in vivo, we examined the rhesus model and sequenced and characterized the rhesus **CMV** US28 locus. We found that rhesus **CMV** carries five tandem homologs of US28, all widely divergent from US28 and from each other. By reverse transcription-PCR and Northern analysis, we demonstrated expression of these ORFs in infected cells. With stable cell lines expressing these ORFs, we analyzed the homolog's binding and signaling characteristics across a wide range of chemokines and found one (RhUS28.5) to have a ligand binding profile similar to that of US28. In addition, we localized US28 and the rhesus **CMV** homolog RhUS28.5 to the envelope of infectious virions, suggesting a role in viral entry or cell tropism.
CT Check Tags: Animal; Human
Amino Acid Sequence
Calcium: ME, metabolism
Chromosome Mapping
Immediate-Early Proteins: GE, genetics

*Macaca mulatta: VI, virology
Molecular Sequence Data
Open Reading Frames
Receptors, Chemokine: CH, chemistry
*Receptors, Chemokine: GE, genetics
Receptors, Chemokine: PH, physiology
Viral Proteins: CH, chemistry
*Viral Proteins: GE, genetics
Viral Proteins: PH, physiology
RN 7440-70-2 (Calcium)
CN 0 (Immediate-Early Proteins); 0 (Receptors, Chemokine); 0 (US28 receptor); 0 (US3 protein, **cytomegalovirus**); 0 (Viral Proteins)

L45 ANSWER 2 OF 16 MEDLINE on STN DUPLICATE 2
AN 2003572736 MEDLINE
DN PubMed ID: 14644603
TI A macrophage inflammatory protein homolog encoded by guinea pig **cytomegalovirus** signals via CC chemokine receptor 1.
AU **Penfold Mark**; Miao Zhenhua; Wang Yu; Haggerty Shannon; Schleiss Mark R
CS ChemoCentryx, San Carlos, CA 94070, USA.
NC HD044864-01 (NICHD)
SO Virology, (2003 Nov 25) 316 (2) 202-12.
Journal code: 0110674. ISSN: 0042-6822.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200401
ED Entered STN: 20031216
Last Updated on STN: 20040107
Entered Medline: 20040106
AB **Cytomegaloviruses** encode homologs of cellular immune effector proteins, including chemokines (CKs) and CK receptor-like G protein-coupled receptors (GPCRs). Sequence of the guinea pig **cytomegalovirus** (GPCMV) genome identified an open reading frame (ORF) which predicted a 101 amino acid (aa) protein with homology to the macrophage inflammatory protein (MIP) subfamily of CC (beta) CKs, designated GPCMV-MIP. To assess functionality of this CK, recombinant GPCMV-MIP was expressed in HEK293 cells and assayed for its ability to bind to and functionally interact with a variety of GPCRs. Specific signaling was observed with the hCCR1 receptor, which could be blocked with hMIP -1alpha in competition experiments. Migration assays revealed that GPCMV-MIP was able to induce chemotaxis in hCCR1-L1.2 cells. Antisera raised against a GST-MIP fusion protein immunoprecipitated species of approximately 12 and 10 kDa from GPCMV-inoculated tissue culture lysates, and convalescent antiserum from GPCMV-infected animals was immunoreactive with GST-MIP by ELISA assay. These results represent the first substantive in vitro characterization of a functional CC CK encoded by a **cytomegalovirus**.
CT Check Tags: Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.
Amino Acid Sequence
Animals
Calcium: ME, metabolism
Cell Movement
Guinea Pigs
Macrophage Inflammatory Proteins: CH, chemistry
Macrophage Inflammatory Proteins: GE, genetics
*Macrophage Inflammatory Proteins: PH, physiology
Molecular Sequence Data
*Receptors, Chemokine: PH, physiology
Roseolovirus: GE, genetics
***Roseolovirus: IM, immunology**

*Signal Transduction: PH, physiology
Viral Proteins: CH, chemistry
Viral Proteins: GE, genetics
*Viral Proteins: PH, physiology
RN 7440-70-2 (Calcium)
CN 0 (CC chemokine receptor 1); 0 (Macrophage Inflammatory Proteins); 0 (Receptors, Chemokine); 0 (Viral Proteins)

L45 ANSWER 3 OF 16 MEDLINE on STN DUPLICATE 3
AN 2002051344 MEDLINE
DN PubMed ID: 11773404
TI Potent immunosuppressive activities of **cytomegalovirus**-encoded interleukin-10.
CM Erratum in: J Virol 2002 Apr;76(7):3585
AU Spencer Juliet V; Lockridge Kristen M; Barry Peter A; Lin Gaofeng; Tsang Monica; **Penfold Mark E T; Schall Thomas J**
CS ChemoCentryx, San Carlos, California 94070, USA.
NC 1-R01-HL57883 (NHLBI)
SO Journal of virology, (2002 Feb) 76 (3) 1285-92.
Journal code: 0113724. ISSN: 0022-538X.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200202
ED Entered STN: 20020125
Last Updated on STN: 20020420
Entered Medline: 20020212
AB **Cytomegalovirus** (**CMV**) has highly evolved mechanisms for avoiding detection by the host immune system. Recently, in the genomes of human and primate **CMV**, a novel gene comprising segments of noncontiguous open reading frames was identified and found to have limited predicted homology to endogenous cellular interleukin-10 (IL-10). Here we investigate the biological activities of the **CMV** IL-10-like gene product and show it to possess potent immunosuppressive properties. Both purified bacterium-derived recombinant **CMV** IL-10 and **CMV** IL-10 expressed in supernatants of human cells were found to inhibit proliferation of mitogen-stimulated peripheral blood mononuclear cells (PBMCs), with specific activity comparable to that of recombinant human IL-10. In addition, **CMV** IL-10 expressed from human cells inhibited cytokine synthesis, as treatment of stimulated PBMCs and monocytes with **CMV** IL-10 led to a marked decrease in production of proinflammatory cytokines. Finally, **CMV** IL-10 was observed to decrease cell surface expression of both major histocompatibility complex (MHC) class I and class II molecules, while conversely increasing expression of the nonclassical MHC allele HLA-G. These results demonstrate for the first time that **CMV** has a biologically active IL-10 homolog that may contribute to immune evasion during virus infection.
CT Check Tags: Human; Support, U.S. Gov't, P.H.S.
Animals
Cell Division
Cell Membrane: IM, immunology
Cells, Cultured
***Cytomegalovirus: ME, metabolism**
Gene Expression
Genes, MHC Class I
Genes, MHC Class II
*Immunosuppressive Agents
Interferon Type II: BI, biosynthesis
*Interleukin-10: ME, metabolism
Leukocytes, Mononuclear: CY, cytology
Leukocytes, Mononuclear: DE, drug effects

Leukocytes, Mononuclear: ME, metabolism
Macaca mulatta
Receptors, Interleukin: ME, metabolism
Recombinant Proteins: ME, metabolism
Viral Proteins: GE, genetics
*Viral Proteins: ME, metabolism
Viral Proteins: PD, pharmacology
RN 130068-27-8 (Interleukin-10); 82115-62-6 (Interferon Type II)
CN 0 (**CMV** IL-10 protein, **Cytomegalovirus**); 0 (Immunosuppressive Agents); 0 (Receptors, Interleukin); 0 (Recombinant Proteins); 0 (Viral Proteins); 0 (interleukin-10 receptor)

L45 ANSWER 4 OF 16 MEDLINE on STN DUPLICATE 4
AN 2001296913 MEDLINE
DN PubMed ID: 11376481
TI A review of genetic differences between limited and extensively passaged human **cytomegalovirus** strains.
AU Prichard M N; **Penfold M E**; Duke G M; Spaete R R; Kemble G W
CS Aviron, 297 N. Bernardo Avenue, Mountain View, CA 94043, USA.
SO Reviews in medical virology, (2001 May-Jun) 11 (3) 191-200. Ref: 71
Journal code: 9112448. ISSN: 1052-9276.
CY England: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 200107
ED Entered STN: 20010716
Last Updated on STN: 20010716
Entered Medline: 20010712
AB The complete genetic content of human **cytomegalovirus** (HCMV) has been difficult to determine, since most strains studied in the laboratory have been extensively passaged in human fibroblast cultures which can change the genetic content as well as the biological properties of the virus. Approximately 13 kb of novel DNA sequences located near the right edge of the unique long (UL) component of the genome has been discovered in Toledo, clinical isolates and certain stocks of Towne. This region of novel sequence, designated the UL/b' region, encodes several interesting proteins including vCXC-1, a potent IL-8 homologue, and UL144, a member of the TNF receptor family. This region is missing from the prototypic laboratory variants of Towne and AD169. In contrast to Toledo and other low passage isolates which have relatively small repeats bracketing the UL component, the Towne and AD169 laboratory variants contain large (>10 kb) b/b' repeats. The large size of these repeats in AD169 and Towne appear to have arisen as compensation for the loss of sequences from the UL/b' region that existed in less passaged variants of these strains. Consequently, many of the haploid genes at the left edge of the prototypic wild-type (wt) UL component are diploid in AD169 and Towne. We hypothesise that this plasticity of the genome at the right edge of the UL component results from extensive passage and adaptation to replication in fibroblasts in vitro. Further work will be required to understand the complete genetic content of wt HCMV.

CT Check Tags: Comparative Study; Human
Amino Acid Sequence
Cells, Cultured
Chemokines, CXC: GE, genetics
***Cytomegalovirus: GE, genetics**
Cytomegalovirus: GD, growth & development
Cytomegalovirus: PY, pathogenicity
Cytomegalovirus Infections: VI, virology
Fibroblasts

*Genome, Viral
Membrane Glycoproteins: GE, genetics
Molecular Sequence Data
Sequence Alignment
Variation (Genetics)
Viral Proteins: GE, genetics
Virus Cultivation
Virus Replication
CN 0 (Chemokines, CXC); 0 (Membrane Glycoproteins); 0 (UL144 ORF protein, Human herpesvirus 5); 0 (Viral Proteins); 0 (viral chemokine CXC-1)

L45 ANSWER 5 OF 16 MEDLINE on STN DUPLICATE 5
AN 1999415953 MEDLINE
DN PubMed ID: 10485920
TI **Cytomegalovirus**-encoded beta chemokine promotes monocyte-associated viremia in the host.
AU Saederup N; Lin Y C; Dairaghi D J; **Schall T J**; Mocarski E S
CS Department of Microbiology and Immunology, Stanford University Medical School, Stanford, CA 94305-5124, USA.
NC RO1 AI28341 (NIAID)
RO1 AI30363 (NIAID)
T32 GM07328 (NIGMS)
SO Proceedings of the National Academy of Sciences of the United States of America, (1999 Sep 14) 96 (19) 10881-6.
Journal code: 7505876. ISSN: 0027-8424.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199910
ED Entered STN: 19991026
Last Updated on STN: 19991026
Entered Medline: 19991014
AB Chemokine homologs are encoded by many large DNA viruses, suggesting that they contribute to control of host leukocyte transmigration and trafficking during viral infection. Murine **cytomegalovirus** carries a CC (beta) chemokine homolog gene giving rise to two related proteins, murine **cytomegalovirus** chemokine 1 and 2 (MCK-1 and MCK-2). MCK-1 peptide was found to induce calcium signaling and adherence in murine peritoneal macrophages. Cells bearing human chemokine receptor CCR3 and the human macrophage THP1 cell line were responsive to MCK-1. This pattern suggested that MCK-1 might act as an agonist, promoting leukocyte trafficking during viral infection. Consistent with this prediction, MCK-1/MCK-2 mutant viruses exhibit dramatically reduced peak levels of monocyte-associated viremia in experimentally infected mice. Thus, MCK-1/MCK-2 appears to promote host leukocyte migration to initial sites of infection and may be responsible for attracting monocytes or macrophages that efficiently disseminate virus in the host.
CT Check Tags: Human; Support, U.S. Gov't, P.H.S.
Amino Acid Sequence
Animals
Calcium: ME, metabolism
*Chemokines: GE, genetics
*Chemokines: ME, metabolism
Chemokines, CC: GE, genetics
*Chemokines, CC: PH, physiology
***Cytomegalovirus: GE, genetics**
Cytomegalovirus: ME, metabolism
Mice
Mice, Inbred BALB C
Models, Biological
Models, Genetic
Molecular Sequence Data

*Monocytes: ME, metabolism
Monocytes: VI, virology
Peritoneum: ME, metabolism
Peritoneum: VI, virology
Recombination, Genetic
Sequence Homology, Amino Acid
Time Factors
*Viremia: GE, genetics
Viremia: ME, metabolism
RN 7440-70-2 (Calcium)
CN 0 (Chemokines); 0 (Chemokines, CC); 0 (MCK-1 protein); 0 (MCK-2 protein, Mouse **cytomegalovirus** 1)

L45 ANSWER 6 OF 16 MEDLINE on STN DUPLICATE 6
AN 1999380606 MEDLINE
DN 99380606 PubMed ID: 10449781
TI **Cytomegalovirus** encodes a potent alpha chemokine.
AU **Penfold M E**; Dairaghi D J; Duke G M; Saederup N; Mocarski E S; Kemble G W; **Schall T J**
CS Aviron, 297 Bernardo Avenue, Mountain View, CA 94043, USA.. mpenfold@aviron.com
NC AI30363 (NIAID)
SO PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (1999 Aug 17) 96 (17) 9839-44.
Journal code: 7505876. ISSN: 0027-8424.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
OS GENBANK-U33331
EM 199909
ED Entered STN: 19990925
Last Updated on STN: 19990925
Entered Medline: 19990909
AB **Cytomegalovirus** is a widespread opportunistic pathogen affecting immunocompromised individuals in whom neutrophils may mediate virus dissemination and contribute to progression of disease. Recent sequence analysis suggests that genes absent or altered in attenuated strains may influence pathogenesis. We have found two genes, UL146 and UL147, whose products have sequence similarity to alpha (CXC) chemokines. UL146 encodes a protein, designated vCXC-1, that is a 117-aa glycoprotein secreted into the culture medium as a late gene product, where its presence correlates with the ability to attract human neutrophils. Recombinant vCXC-1 is a fully functional chemokine, inducing calcium mobilization, chemotaxis, and degranulation of neutrophils. High-affinity vCXC-1 binding is shown to be mediated via CXCR2, but not CXCR1. vCXC-1 exhibits a potency approaching that of human IL-8. As the first example of a virus-encoded alpha chemokine, vCXC-1 may ensure the active recruitment of neutrophils during **cytomegalovirus** infection, thereby providing for efficient dissemination during acute infection and accounting for the prominence of this leukocyte subset in **cytomegalovirus** disease.
CT Check Tags: Human; Support, U.S. Gov't, P.H.S.
Amino Acid Sequence
Chemokines, CXC: CH, chemistry
Chemokines, CXC: GE, genetics
*Chemokines, CXC: ME, metabolism
Cloning, Molecular
Cytomegalovirus: GE, genetics
***Cytomegalovirus: ME, metabolism**
***Cytomegalovirus Infections: ME, metabolism**
DNA, Viral: CH, chemistry
Fibroblasts: ME, metabolism

Fibroblasts: VI, virology
Lung: CY, cytology
Molecular Sequence Data
*Receptors, Chemokine: ME, metabolism
*Receptors, Interleukin: ME, metabolism
Receptors, Interleukin-8B
CN 0 (Chemokines, CXC); 0 (DNA, Viral); 0 (Receptors, Chemokine); 0 (Receptors, Interleukin); 0 (Receptors, Interleukin-8B); 0 (viral chemokine CXC-1)

L45 ANSWER 7 OF 16 MEDLINE on STN DUPLICATE 7
AN 1998406221 MEDLINE
DN 98406221 PubMed ID: 9733857
TI Functional analysis of the human **cytomegalovirus** US28 gene by insertion mutagenesis with the green fluorescent protein gene.
AU Vieira J; **Schall T J**; Corey L; Geballe A P
CS Department of Laboratory Medicine, University of Washington, Seattle, Washington 98195, USA.. vieiraj@u.washington.edu
NC AI26672 (NIAID)
SO JOURNAL OF VIROLOGY, (1998 Oct) 72 (10) 8158-65.
Journal code: 0113724. ISSN: 0022-538X.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199810
ED Entered STN: 19981020
Last Updated on STN: 19981020
Entered Medline: 19981007
AB The protein encoded by the US28 gene of human **cytomegalovirus** (HCMV) has homology to G protein-coupled receptors (GCR). Previous studies demonstrated that recombinant US28 protein can bind the beta class of chemokines (K. Neote, D. DiGregorio, J. Y. Mak, R. Horuk, and T. J. Schall, Cell 72:415-425, 1993) and induce a rise in intracellular calcium after the binding of chemokines (J. L. Gao and P. M. Murphy, J. Biol. Chemical 269:28539-28542, 1994). In order to investigate the function of the US28 protein in virus-infected cells, a recombinant HCMV (HV5.8) was constructed, with the US28 open reading frame disrupted by the insertion of the Escherichia coli gpt gene and the gene for the green fluorescent protein. The US28 gene is not required for growth in human fibroblasts (HF). HF infected with wild-type HCMV bound RANTES at 24 h postinfection and demonstrated an intracellular calcium flux induced by RANTES. In cells infected with HV5.8, RANTES did not bind or induce a calcium flux, demonstrating that US28 is responsible for the beta-chemokine binding and induced calcium signaling in HCMV-infected cells. The ability of the US28 gene to bind chemokines was shown to cause a significant reduction in the concentration of RANTES in the medium of infected cells. Northern analysis of RNA from infected cells showed that US28 is an early gene, while US27 (another GCR) is a late gene.
CT Check Tags: Human; Support, U.S. Gov't, P.H.S.
Blotting, Northern
Calcium: ME, metabolism
Cells, Cultured
***Cytomegalovirus: GE, genetics**
Ion Transport
*Luminescent Proteins: GE, genetics
Mutagenesis, Site-Directed
RANTES: ME, metabolism
RNA, Viral: GE, genetics
*Receptors, Chemokine: GE, genetics
Receptors, Chemokine: ME, metabolism
Recombinant Proteins: GE, genetics
RN 147336-22-9 (green fluorescent protein); 156286-78-1 (monocyte

chemoattractant protein 1 receptor); 7440-70-2 (Calcium)
CN 0 (Luminescent Proteins); 0 (RANTES); 0 (RNA, Viral); 0 (Receptors, Chemokine); 0 (Recombinant Proteins)

L45 ANSWER 8 OF 16 MEDLINE on STN DUPLICATE 8
AN 1998362100 MEDLINE
DN 98362100 PubMed ID: 9696791
TI Identification of persistent RNA-DNA hybrid structures within the origin of replication of human **cytomegalovirus.**
AU Prichard M N; Jairath S; **Penfold M E;** St Jeor S; Bohlman M C; Pari G S
CS Iconix Pharmaceuticals, Inc., Mountain View, California 94043, USA.
SO JOURNAL OF VIROLOGY, (1998 Sep) 72 (9) 6997-7004.
Journal code: 0113724. ISSN: 0022-538X.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199809
ED Entered STN: 19980925
Last Updated on STN: 19980925
Entered Medline: 19980916
AB Human **cytomegalovirus** (HCMV) lytic-phase DNA replication initiates at the cis-acting origin of replication, oriLyt. oriLyt is a structurally complex region containing repeat elements and transcription factor binding sites. We identified two site-specific alkali-labile regions within oriLyt which flank an alkali-resistant DNA segment. These alkali-sensitive regions were the result of the degradation of two RNA species embedded within oriLyt and covalently linked to viral DNA. The virus-associated RNA, vRNA, was identified by DNase I treatment of HCMV DNA obtained from sucrose gradient purified virus. This heterogeneous population of vRNA was end labeled and used as a hybridization probe to map the exact location of vRNAs within oriLyt. vRNA-1 is localized between restriction endonuclease sites XhoI at nucleotide (nt) 93799 and SacI at nt 94631 and is approximately 500 bases long. The second vRNA, vRNA-2, lies within a region which exhibits a heterogeneous restriction pattern located between the SphI (nt 92636) and BamHI (nt 93513) and is approximately 300 bases long. This region was previously shown to be required for oriLyt replication (D. G. Anders, M. A. Kacica, G. S. Pari, and S. M. Punturieri, J. Virol. 66:3373-3384, 1992). RNase H analysis determined that vRNA-2 forms a persistent RNA-DNA hybrid structure in the context of the viral genome and in an oriLyt-containing plasmid used in the transient-replication assay.
CT Check Tags: Human
Binding Sites
Cell Line
Chromosome Mapping
***Cytomegalovirus: GE, genetics**
*DNA, Viral
Nucleic Acid Conformation
*RNA, Viral
*Recombination, Genetic
*Replication Origin
Restriction Mapping
Sodium Hydroxide
RN 1310-73-2 (Sodium Hydroxide)
CN 0 (DNA, Viral); 0 (RNA, Viral)

L45 ANSWER 9 OF 16 MEDLINE on STN DUPLICATE 9
AN 1998087825 MEDLINE
DN 98087825 PubMed ID: 9426445
TI Formation of **cytomegalovirus** DNA replication compartments defined by localization of viral proteins and DNA synthesis.

AU **Penfold M E**; Mocarski E S
CS Department of Microbiology and Immunology, Stanford University, California 94305-5124, USA.
NC AI20211 (NIAID)
SO VIROLOGY, (1997 Dec 8) 239 (1) 46-61.
Journal code: 0110674. ISSN: 0042-6822.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199801
ED Entered STN: 19980206
Last Updated on STN: 19980206
Entered Medline: 19980129
AB To characterize the formation of replication compartments in human **cytomegalovirus**-infected cells, and to determine the fate of newly synthesized DNA, we localized viral replication proteins and DNA synthesis at early and late times during infection. As expected, ppUL57 (single-stranded DNA binding protein) and ppUL44 (DNA polymerase processivity factor) both localized to replication compartments beginning at 48 hpi. BrdU was incorporated into viral DNA in these compartments that was found to mature into progeny virus based on our ability to chase the label into the cytoplasm and out of the cell over the ensuing 72-h period. Although the pattern of BrdU incorporation at early times (20 or 24 hpi) was punctate, and distinct from the replication compartment that formed later during infection, viral DNA synthesized at this time also matured into progeny virus during a chase. Interestingly, sites of ppUL57 localization did not overlap completely with sites of BrdU incorporation at early times. Products from the UL112-113 gene localized to subnuclear regions by 6 hpi, earlier than ppUL57. Between 12 and 24 hpi, both ppUL57 and ppUL44 joined UL112-113 gene products at sites that subsequently developed into replication compartments. When infection was carried out in the presence of phosphonoformate or ganciclovir, replication compartment formation was blocked. A viral mutant deficient in uracil DNA glycosidase, previously shown to exhibit a delay in the initial phase of DNA replication, also exhibited delayed formation of replication compartments. These results raise the possibility that subnuclear sites defined by UL112-113 localization orchestrate the assembly of the **CMV** replication compartment and implicate punctate sites of BrdU incorporation as sites of early viral DNA replication that precedes the formation of the replication compartment.
CT Check Tags: Human; Support, U.S. Gov't, P.H.S.
Cell Compartmentation
Cell Line
***Cytomegalovirus: PH, physiology**
*DNA Replication
*DNA, Viral: GE, genetics
Microscopy, Confocal
*Viral Proteins: PH, physiology
Virus Replication
CN 0 (DNA, Viral); 0 (Viral Proteins)

L45 ANSWER 10 OF 16 MEDLINE on STN DUPLICATE 10
AN 93161416 MEDLINE
DN 93161416 PubMed ID: 7679328
TI Molecular cloning, functional expression, and signaling characteristics of a C-C chemokine receptor.
AU Neote K; DiGregorio D; Mak J Y; Horuk R; **Schall T J**
CS Department of Immunology, Genentech, Incorporated, South San Francisco, California 94080.
SO CELL, (1993 Feb 12) 72 (3) 415-25.
Journal code: 0413066. ISSN: 0092-8674.
CY United States

DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
OS GENBANK-L09230; GENBANK-L20501; GENBANK-L33702; GENBANK-L33703; GENBANK-L33704; GENBANK-L33705; GENBANK-L33706; GENBANK-L33707; GENBANK-L33708; GENBANK-L33709; GENBANK-M99293; GENBANK-X17403
EM 199303
ED Entered STN: 19930402
Last Updated on STN: 19970203
Entered Medline: 19930316
AB The immunoregulatory proteins C-C chemokines are potent chemoattractants of lymphocytes and monocytes, as well as activators and attractants of eosinophils and basophils. We have isolated a cDNA that encodes a seven transmembrane-spanning receptor, with homology to other chemoattractant receptors, that encodes a protein designated C-C CKR-1 that acts as a receptor for the C-C chemokines. Human and murine macrophage inflammatory protein 1 alpha (MIP-1 alpha), human human monocyte chemotactic protein 1 (MCP-1), and RANTES all bind to the C-C CKR-1 with varying affinities. Chemokine binding affinity does not predict how well the ligand will transmit a signal through the receptor: RANTES and human MIP-1 alpha induce a similar intracellular calcium flux while binding with disparate affinities, while MCP-1 and human MIP-1 beta induce calcium mobilization only at high concentrations. Finally, C-C chemokines were shown to bind a C-C CKR-1-related gene product encoded by **cytomegalovirus**, suggesting a role for C-C chemokines in viral immunity.
CT Check Tags: Human; In Vitro
Amino Acid Sequence
Binding, Competitive
Calcium: PH, physiology
Cells, Cultured
Cloning, Molecular
*Cytokines: PH, physiology
Cytomegalovirus: ME, metabolism
DNA: GE, genetics
Genes, Structural, Viral
*Lymphokines: PH, physiology
Macrophage Inflammatory Protein-1
Molecular Sequence Data
*Monokines: PH, physiology
Oligopeptides: CH, chemistry
Open Reading Frames
RANTES
*Receptors, Cell Surface: GE, genetics
Receptors, Cell Surface: PH, physiology
Sequence Alignment
Signal Transduction
Viral Proteins: ME, metabolism
RN 7440-70-2 (Calcium); 9007-49-2 (DNA)
CN 0 (Cytokines); 0 (Lymphokines); 0 (Macrophage Inflammatory Protein-1); 0 (Monokines); 0 (Oligopeptides); 0 (RANTES); 0 (Receptors, Cell Surface); 0 (Viral Proteins)
GEN C5AR; CKR-1; FMLPR; IL8RA; IL8RB; STSR

L45 ANSWER 11 OF 16 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
AN 2003:260926 BIOSIS
DN PREV200300260926
TI A novel **cytomegalovirus**-encoded chemokine signals via CC chemokine receptor 1 (CCR1).
AU Schleiss, Mark R. [Reprint Author]; Haggerty, Shannon; Wang, Yu; Miao, Zhenua; **Penfold, Mark**
CS Division of Infectious Diseases, Children's Hospital Research Foundation, Cincinnati, OH, USA
SO Pediatric Research, (April 2003) Vol. 53, No. 4 Part 2, pp. 349A. print.

Meeting Info.: Annual Meeting of the Pediatric Academic Societies'. Seattle, WA, USA. May 03-06, 2003. Pediatric Academic Societies. ISSN: 0031-3998 (ISSN print).
DT Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LA English
ED Entered STN: 4 Jun 2003
Last Updated on STN: 4 Jun 2003
CC General biology - Symposia, transactions and proceedings 00520
Genetics - General 03502
Genetics - Animal 03506
Genetics - Human 03508
Endocrine - General 17002
Genetics of bacteria and viruses 31500
Virology - General and methods 33502
Medical and clinical microbiology - Virology 36006
IT Major Concepts
Infection; Molecular Genetics (Biochemistry and Molecular Biophysics)
IT Diseases
cytomegalovirus infection: viral disease
Cytomegalovirus Infections (MeSH)
IT Chemicals & Biochemicals
CC chemokine receptor 1; chemokines; macrophage inflammatory protein-1-alpha
IT Miscellaneous Descriptors
viral genome
ORGN Classifier
Herpesviridae 03115
Super Taxa
dsDNA Viruses; Viruses; Microorganisms
Organism Name
Cytomegalovirus (genus): pathogen
Taxa Notes
Double-Stranded DNA Viruses, Microorganisms, Viruses
ORGN Classifier
Hominidae 86215
Super Taxa
Primates; Mammalia; Vertebrata; Chordata; Animalia
Organism Name
HEK293 cell line (cell line)
Taxa Notes
Animals, Chordates, Humans, Mammals, Primates, Vertebrates
ORGN Classifier
Caviidae 86300
Super Taxa
Rodentia; Mammalia; Vertebrata; Chordata; Animalia
Organism Name
guinea-pig (common): host, animal model
Taxa Notes
Animals, Chordates, Mammals, Nonhuman Vertebrates, Nonhuman Mammals, Rodents, Vertebrates
GEN **cytomegalovirus** MIP gene [**cytomegalovirus** macrophage inflammatory protein gene] (Herpesviridae): deletion

L45 ANSWER 12 OF 16 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
AN 2000:493692 BIOSIS
DN PREV200000493813
TI Interplay between the 'endogenous' and 'infectious' chemokine systems.
AU **Schall, Thomas** [Reprint author]
CS ChemoCentryx, San Carlos, CA, USA
SO Journal of Human Virology, (September-October, 2000) Vol. 3, No. 5, pp. 239. print.
Meeting Info.: 2000 International Meeting of the Institute of Human

Virology. Baltimore, Maryland, USA. September 10-15, 2000.
ISSN: 1090-9508.
DT Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LA English
ED Entered STN: 15 Nov 2000
Last Updated on STN: 10 Jan 2002
CC Endocrine - General 17002
General biology - Symposia, transactions and proceedings 00520
Pathology - General 12502
Virology - Animal host viruses 33506
Immunology - General and methods 34502
Immunology - Immunopathology, tissue immunology 34508
Medical and clinical microbiology - Virology 36006
IT Major Concepts
Immune System (Chemical Coordination and Homeostasis); Infection
IT Diseases
autoimmune disease: immune system disease
Autoimmune Diseases (MeSH)
IT Chemicals & Biochemicals
chemokine systems: analysis, endogenous, functions, infectious, interplay; chemokines
IT Miscellaneous Descriptors
autoimmunity; infections; inflammation; pathology; therapeutic intervention: molecular targets; Meeting Abstract
ORGN Classifier
Herpesviridae 03115
Super Taxa
dsDNA Viruses; Viruses; Microorganisms
Organism Name
cytomegalovirus
human herpesvirus-8: pathogen
Taxa Notes
Double-Stranded DNA Viruses, Microorganisms, Viruses
ORGN Classifier
Hominidae 86215
Super Taxa
Primates; Mammalia; Vertebrata; Chordata; Animalia
Organism Name
human: host
Taxa Notes
Animals, Chordates, Humans, Mammals, Primates, Vertebrates

L45 ANSWER 13 OF 16 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
AN 1999:470347 BIOSIS
DN PREV199900470347
TI HHV8-encoded vMIP-I selectively engages chemokine receptor CCR8. Agonist and antagonist profiles of viral chemokines.
AU Dairaghi, Daniel J.; Fan, Rong A.; McMaster, Brian E.; Hanley, Michael R.; **Schall, Thomas J.** [Reprint author]
CS ChemoCentryx, 1539 Industrial Rd., San Carlos, CA, 94070, USA
SO Journal of Biological Chemistry, (July 30, 1999) Vol. 274, No. 31, pp. 21569-21574. print.
CODEN: JBCHA3. ISSN: 0021-9258.
DT Article
LA English
ED Entered STN: 9 Nov 1999
Last Updated on STN: 9 Nov 1999
AB Uncertainty regarding viral chemokine function is mirrored by an incomplete knowledge of host chemokine receptor usage by the virally encoded proteins. One such molecule is vMIP-I, a C-C type chemokine of undefined function and binding specificity, encoded by the Kaposi's sarcoma herpesvirus HHV-8. We report here that vMIP-I binds to and

induces cytosolic (Ca2+) signals in human T cells selectively through CCR8, a CC chemokine receptor associated with Th2 lymphocytes. Furthermore, using a panel of 65 different human, viral, and rodent chemokines, we have established a comprehensive ligand binding "fingerprint" for CCR8. The receptor exhibits marked "high" affinity (Kd < 15 nM) only for four chemokines, three of them of viral origin: vMIP-I, vMIP-II, vMCC-I, and human I-309. A previously unreported second class of lower affinity ligands includes MCP-3 and possibly two other viral chemokines. vMIP-I and I-309 appear to act as CCR8 agonists: binding to and inducing cytosolic (Ca2+) elevation through the receptor. By contrast, vMIP-II and vMCC-I act as potent antagonists: binding without inducing signaling, and blocking the effects of I-309 and vMIP-I. These results suggest a ligand hierarchy for CCR8, identifying vMIP-I as a selective viral chemokine agonist. CCR8 may thus engage a specific subset of chemokines with the potential to regulate each other during viral infection and immune regulation.

CC Medical and clinical microbiology - General and methods 36001
Biochemistry studies - General 10060
Enzymes - General and comparative studies: coenzymes 10802
Blood - General and methods 15001
Immunology - General and methods 34502
General biology - Miscellaneous 00532

IT Major Concepts
Enzymology (Biochemistry and Molecular Biophysics); Infection

IT Parts, Structures, & Systems of Organisms
CCR8 chemokine receptor; Th2 lymphocyte: blood and lymphatics, immune system

IT Chemicals & Biochemicals
viral chemokines: agonist profile, antagonist profile; vMIP-II; vMIP-1

ORGN Classifier
Herpesviridae 03115
Super Taxa
dsDNA Viruses; Viruses; Microorganisms
Organism Name
human herpesvirus 8
Taxa Notes
Double-Stranded DNA Viruses, Microorganisms, Viruses

L45 ANSWER 14 OF 16 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
AN 1996:66311 BIOSIS
DN PREV199698638446
TI Herpes simplex virus protein targets for CD4 and CD8 lymphocyte cytotoxicity in cultured epidermal keratinocytes treated with interferon-gamma.
AU Mikloska, Zorka; Kesson, Alison M.; **Penfold, Mark E. T.**; Cunningham, Anthony L. [Reprint author]
CS Virol. Dep., ICPMR, Westmead Hosp., Westmead NSW 2145, Australia
SO Journal of Infectious Diseases, (1996) Vol. 173, No. 1, pp. 7-17. CODEN: JIDIAQ. ISSN: 0022-1899.
DT Article
LA English
ED Entered STN: 9 Feb 1996
Last Updated on STN: 9 Feb 1996
AB In early recurrent herpetic lesions, CD4 T lymphocytes are the predominant infiltrating cells, and keratinocytes expressing major histocompatibility complex (MHC) class II antigens, induced by interferon-gamma (IFN-gamma), are the major site of herpes simplex virus (HSV) replication. IFN-gamma pretreatment of human keratinocytes in vitro reduced MHC class I antigen down-regulation by HSV-1 infection and induced expression of HLA-DR that was unaltered by subsequent HSV-1 infection. Incubation of these infected keratinocytes with phosphonoacetic acid (PAA) almost completely inhibited expression of four major HSV glycoproteins, although expression of early proteins was not affected. Weak CD8 T lymphocyte cytotoxicity against

IFN-gamma-stimulated, HLA-DR-expressing HSV-1-infected keratinocytes was consistently directed to the immediate early/early proteins (all 9 patients tested) but against late proteins to a lesser degree (4/9 patients). However, CD4 T lymphocyte cytotoxicity was much greater and directed predominantly against late HSV-1 glycoproteins (all 9 subjects tested) in these cells.

CC Cytology - Human 02508
Biochemistry studies - Proteins, peptides and amino acids 10064
Blood - Lymphatic tissue and reticuloendothelial system 15008
Pharmacology - Immunological processes and allergy 22018
In vitro cellular and subcellular studies 32600
Immunology - Bacterial, viral and fungal 34504
Medical and clinical microbiology - Virology 36006

IT Major Concepts
Blood and Lymphatics (Transport and Circulation); Cell Biology; Immune System (Chemical Coordination and Homeostasis); Infection; Pharmacology

IT Miscellaneous Descriptors
IMMUNOLOGIC-DRUG; INTERFERON-GAMMA; MAJOR HISTOCOMPATIBILITY COMPLEX

ORGN Classifier
Herpesviridae 03115
Super Taxa
dsDNA Viruses; Viruses; Microorganisms
Organism Name
Herpesviridae
Taxa Notes
Double-Stranded DNA Viruses, Microorganisms, Viruses

ORGN Classifier
Hominidae 86215
Super Taxa
Primates; Mammalia; Vertebrata; Chordata; Animalia
Organism Name
human
Taxa Notes
Animals, Chordates, Humans, Mammals, Primates, Vertebrates

L45 ANSWER 15 OF 16 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
AN 1994:392567 BIOSIS
DN PREV199497405567
TI Axonal transport of herpes simplex virions to epidermal cells: Evidence for a specialized mode of virus transport and assembly.
AU **Penfold, Mark E. T.**; Armati, Patricia; Cunningham, Anthony L. [Reprint author]
CS Virol. Dep., Inst., Clinical Pathol. Med. Research, Westmead Hosp., Westmead 2145 New South Wales, Australia
SO Proceedings of the National Academy of Sciences of the United States of America, (1994) Vol. 91, No. 14, pp. 6529-6533.
CODEN: PNASA6. ISSN: 0027-8424.
DT Article
LA English
ED Entered STN: 14 Sep 1994
Last Updated on STN: 14 Sep 1994
AB To examine the transmission of herpes simplex virus (HSV) from axon to epidermal cell, an in vitro model was constructed consisting of human fetal dorsal root ganglia cultured in the central chamber of a dual-chamber tissue culture system separated from autologous skin explants in an exterior chamber by concentric steel cylinders adhering to the substratum through silicon grease and agarose. Axons grew through the agarose viral diffusion barrier and terminated on epidermal cells in the exterior chamber. After inoculation of HSV onto dorsal root ganglia, anterograde axonal transport of glycoprotein and nucleocapsid antigen was observed by confocal microscopy to appear in exterior chamber axons within 12 h and in epidermal cells within 16 h, moving at 2-3 mm/h. Although both enveloped and unenveloped nucleocapsids were observed in the neuronal

soma by transmission electron microscopy, only nucleocapsids were observed in the axons, closely associated with microtubules. Nodule formation at the surface of HSV-infected axons, becoming more dense at the axon terminus on epidermal cells, and patches of axolemmal HSV glycoprotein D expression were observed by scanning (immuno)electron microscopy, probably representing virus emerging from the axolemma. These findings strongly suggest a specialized mode of viral transport, assembly, and egress in sensory neurons: microtubule-associated intermediate-fast anterograde axonal transport of unenveloped nucleocapsids with separate transport of glycoproteins to the distal regions of the axon and assembly prior to virus emergence at the axon terminus.

CC Cytology - Human 02508
Nervous system - Pathology 20506
Routes of immunization, infection and therapy 22100
Virology - Animal host viruses 33506
Medical and clinical microbiology - Virology 36006

IT Major Concepts
Cell Biology; Infection; Microbiology; Neurology (Human Medicine, Medical Sciences)

IT Miscellaneous Descriptors
VIRAL TRANSMISSION

ORGN Classifier
Herpesviridae 03115
Super Taxa
dsDNA Viruses; Viruses; Microorganisms
Organism Name
Herpesviridae
Taxa Notes
Double-Stranded DNA Viruses, Microorganisms, Viruses

ORGN Classifier
Hominidae 86215
Super Taxa
Primates; Mammalia; Vertebrata; Chordata; Animalia
Organism Name
human
Taxa Notes
Animals, Chordates, Humans, Mammals, Primates, Vertebrates

L45 ANSWER 16 OF 16 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
AN 1993:334301 BIOSIS
DN PREV199345029026
TI Molecular cloning, functional expression, and signalling characteristics of a C-C "chemokine" receptor.
AU Neote, Kuldeep; Digregorio, David; Mak, John Y.; Horuk, Richard; **Schall, Thomas J.**
CS Genetech Inc., S. San Francisco, CA 94080, USA
SO Journal of Immunology, (1993) Vol. 150, No. 8 PART 2, pp. 204A.
Meeting Info.: Joint Meeting of the American Association of Immunologists and the Clinical Immunology Society. Denver, Colorado, USA. May 21-25, 1993.
CODEN: JOIMA3. ISSN: 0022-1767.
DT Conference; (Meeting)
LA English
ED Entered STN: 16 Jul 1993
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CC General biology - Symposia, transactions and proceedings 00520
Genetics - Human 03508
Biochemistry studies - Proteins, peptides and amino acids 10064
Biochemistry studies - Minerals 10069
Biophysics - Molecular properties and macromolecules 10506
Biophysics - Membrane phenomena 10508
Movement 12100
Metabolism - General metabolism and metabolic pathways 13002

Metabolism - Proteins, peptides and amino acids 13012
Virology - Animal host viruses 33506
Immunology - Bacterial, viral and fungal 34504
Immunology - Immunopathology, tissue immunology 34508
Medical and clinical microbiology - Virology 36006
IT Major Concepts
Biochemistry and Molecular Biophysics; Clinical Endocrinology (Human Medicine, Medical Sciences); Genetics; Immune System (Chemical Coordination and Homeostasis); Infection; Membranes (Cell Biology); Metabolism; Microbiology
IT Chemicals & Biochemicals
CALCIUM
IT Miscellaneous Descriptors
ABSTRACT; CALCIUM FLUX; CHEMOKINE BINDING AFFINITY; **CYTOMEGALOVIRUS** INFECTION; LIGAND SPECIFICITY; SEVEN-TRANSMEMBRANE-SPANNING RECEPTOR C-C CKR-1
ORGN Classifier
Herpesviridae 03115
Super Taxa
dsDNA Viruses; Viruses; Microorganisms
Organism Name
Herpesviridae
Taxa Notes
Double-Stranded DNA Viruses, Microorganisms, Viruses
ORGN Classifier
Hominidae 86215
Super Taxa
Primates; Mammalia; Vertebrata; Chordata; Animalia
Organism Name
human
Taxa Notes
Animals, Chordates, Humans, Mammals, Primates, Vertebrates
RN 7440-70-2 (CALCIUM)

=> => fil wpix
FILE 'WPIX' ENTERED AT 09:09:04 ON 30 JAN 2004
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FILE LAST UPDATED: 28 JAN 2004 <20040128/UP>
MOST RECENT DERWENT UPDATE: 200407 <200407/DW>
DERWENT WORLD PATENTS INDEX SUBSCRIBER FILE, COVERS 1963 TO DATE

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SDIS USING THE TIME RANGE CODE WILL NEED TO BE UPDATED.
FOR FURTHER DETAILS: http://thomsonderwent.com/chem/polymers/ <<<

=> d all abeq tech abex tot 171

L71 ANSWER 1 OF 2 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN
AN 2002-674849 [72] WPIX
DNC C2002-190054
TI Collection of **cytomegalovirus** or **cytomegalovirus** infected cells involves contacting a compound that binds **cytomegalovirus** or **cytomegalovirus** infected cell with patient's blood.
DC B02 B03 B04 D16
IN **PENFOLD, M E T; SCHALL, T J**
PA (CHEM-N) **CHEMOCENTRYX INC**
CYC 100
PI WO 2002062956 A2 20020815 (200272)* EN 41p C12N000-00
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZM ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG US UZ VN YU ZA ZM ZW
US 2002182594 A1 20021205 (200301) C12Q001-70 <--
ADT WO 2002062956 A2 **WO 2002-US3229 20020201**; US 2002182594 A1 **Provisional US 2001-266094P 20010202**, US 2002-61944 20020201
PRAI **US 2001-266094P 20010202**; US 2002-61944 20020201
IC ICM C12N000-00; C12Q001-70
ICS G01N033-53
AB WO 200262956 A UPAB: 20021108
NOVELTY - Collection (M1) of **cytomegalovirus** (**CMV**) or **CMV** infected cells from a patient by either inserting a support comprising a compound (A), which binds **CMV** or **CMV** infected cells, into the patient's blood system; or contacting the patient's blood or a tissue containing **CMV** or **CMV** infected cells with (A), so that **CMV** or a **CMV** infected cell in the blood is collected by (A), is new.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:
(1) an apparatus comprising a collector having (A) and a circuit for connecting the blood system of a patient and for flowing the withdrawn blood through it and is in fluid communication with the collector; and
(2) assessing mutations in **CMV** involving:
(a) collecting **CMV** and/or at least one **CMV** infected cell from a patient by contacting the blood or a tissue of the patient with (A) so that **CMV** or at least one **CMV** infected cell is bound from the blood or tissue; and
(b) detecting the presence and/or absence of a mutation in **CMV** obtained from the **CMV** or at least one **CMV** infected cell collected in step (2a).
ACTIVITY - Virucide.
No biological data given.
MECHANISM OF ACTION - None given.
USE - M1 is useful for collection of **CMV**, or a **CMV** infected cell from humans, animals (claimed) (e.g. monkey, ape, gorilla and baboon, and commercial livestock (e.g. chicken, pig, sheep and cow); for tracking the dissemination or infection of the host; as an in vivo or ex vivo collection mechanism to measure mutation rates and selective

pressures after in vivo passage; and to remove a virus or recombinant virus from a host (e.g. for therapeutic purposes).

ADVANTAGE - The compound expresses on the surface of both virions and infected cells and is involved in viral dissemination by binding to various chemokines.

Dwg.0/1

FS CPI

FA AB; GI; DCN

MC CPI: B04-B04D5; B04-F02; **B04-F11**; B06-B02; B07-D03; B07-D05; B07-D06; B11-B; B11-C04A; B11-C08E5; B12-K04A3; B12-K04F; B12-M02D; B14-A02A3; **D05-H06**; D05-H10; D05-H13

TECH UPTX: 20021108

TECHNOLOGY FOCUS - INSTRUMENTATION AND TESTING - Preferred Apparatus: The circuit comprises an outlet line and a return line, each in fluid communication with the blood system of the patient, and the circuit is adapted for withdrawal of the blood from the patient's blood system via the outlet line, passage of the blood through the collector and the return of the blood to the blood system via the return line. The compound is contained on a support within the collector. The support is selected from beads, microspheres, nanoparticles, or colloidal particles. The apparatus further comprises a pump for pumping blood through the circuit.

Preferred Device: The support is an implant device for inserting into a patient to contact with the blood of the patient. The implant comprises an absorptive material (preferably a surgical sponge) and is selected from gelfoam, polyester or polyurethane. The support is a patch for applying to the skin.

Preferred Method: Collection of the **CMV** by inserting a support further involves removing the implant device from the patient after **CMV** and/or **CMV** infected cells has accumulated at the implant device. Collection of the **CMV** by contacting the patient's blood or a tissue with compound further involves withdrawing blood containing **CMV** or the **CMV** infected cell from the patient and flowing the blood through or into the collector; and re-circulating the blood back into the patient after the contacting step. The withdrawing, contacting and recirculating steps are performed continuously. The method further involves providing a collection apparatus, the collection apparatus comprising the collector and the circuit; withdrawing the blood from the patient via outlet line and flowing withdrawn blood through the collector; and re-circulating the blood back to the patient via the return line.

The method of assessing mutation involves placing an implant device that contains the compound in or on the patient such that the implant device is contacted with the blood of the patient, in which **CMV** or the at least one **CMV** or the one **CMV** infected cell in the blood is captured by (A) of the implant device. If a mutation is detected, the method further involves determining whether the mutation confers resistance to a pharmaceutical agent. The method further involves administering the pharmaceutical compound to the patient prior to the collection step by placing a transdermal patch containing (A) on the skin of the patient.

TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - The compound is a ligand for **CMV** US28. The compound is of formula Ar-C(O)-NR11-CH2-Nhet (I) or its salt (preferably of formula (Ia), (Ib) or (Ic)).

Ar = substituted aryl group;

R11 and R15 = H or optionally substituted 1-4C alkyl;

Nhet = optionally substituted 4- to 7-membered nitrogen heterocycle;

n and m = 1 - 3;

R12 - R14 = R1 or OH;

X1 - X4 = N or CR1;

R1 - R3 = H, halo, 1-4C alkyl, 1-4C alkoxy, 1-4C haloalkyl, 1-4C haloalkoxy, nitro, cyano, 1-4C acyl, amino, 1-4C alkylamino, or di(1-4C)alkylamino;

Y1 - Y4 = N or CR2;
Z1 = divalent moiety of (1-3C)alkylene;
Z2 = divalent moiety selected from -O-, -S- and -N(R3)-;
R'3 = 1-4C alkyl, 1-4C haloalkyl or 1-4C acyl.

L71 ANSWER 2 OF 2 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN
AN 2002-269444 [31] WPIX
CR 2002-304220 [34]; 2002-351718 [38]
DNC C2002-080027
TI Assay for identifying a compound useful for blocking **cytomegalovirus** dissemination in a host involves determining whether the compound inhibits binding of a chemokine to US28 or its fragment.
DC B02 B03 B04 D16 K08 S03
IN DAIRAGHI, D J; MCMASTER, B E; **SCHALL, T J**
PA (CHEM-N) **CHEMOCENTRYX INC**
CYC 97
PI WO 2002017900 A2 20020307 (200231)* EN 28p A61K031-00
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PH PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 2001087043 A 20020313 (200249) A61K031-00
US 2002127544 A1 20020912 (200262) C12Q001-70
ADT WO 2002017900 A2 WO 2001-US27363 20010830; AU 2001087043 A AU 2001-87043 20010830; US 2002127544 A1 Provisional US 2000-228974P 20000830, Provisional US 2000-229191P 20000830, Provisional US 2000-229365P 20000830, US 2001-944163 20010830
FDT AU 2001087043 A Based on WO 2002017900
PRAI US 2000-228974P 20000830; US 2000-229191P 20000830; US 2000-229365P 20000830; US 2001-944163 20010830
IC ICM A61K031-00; C12Q001-70
ICS A61K031-473; A61K031-498; A61K031-519
AB WO 200217900 A UPAB: 20021001
NOVELTY - An assay for identifying a compound (a), useful for blocking **cytomegalovirus** (**CMV**) involves determining whether (a) inhibits the binding of a chemokine to US28 or a US28 fragment.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for:
(1) preventing dissemination of **cytomegalovirus** (**CMV**) involving administering (a) to block the binding of the chemokine to the US28 or its fragment;
(2) reducing cell motility in a **CMV**-infected cell involving contacting the cell with (a) on the surface of the infected cell; and
(3) a pharmaceutical composition comprising a compound of formula (I) and a carrier.
X1 - X4 = N or C-R1;
R1 = T;
T = H or T1;
T1 = halogen, 1-4C (halo)alkyl, 1-4C (halo)alkoxy, nitro, cyano, 1-4C acyl, amino, 1-4C alkylamino or di(1-4C alkyl)amino;
Y1 - Y4 = N or C-R2 (preferably CH);
R2 = T;
Z1 = a divalent moiety selected from 1-3C alkylene;
Z2 = a divalent moiety selected from -O-, -S- or -N(R3);
R3 = T; and
R = optionally substituted 4 - 7 membered nitrogen heterocycle.
ACTIVITY - Antiviral; Cardiant; Antiinflammatory; Neuroprotective; Vasotropic.
MECHANISM OF ACTION - Chemokine-US28 receptor or a US28 fragment binding inhibitor; **CMV** dissemination blocker. US28 expressing cells consisted of a mouse cell line stably expressing transfected US28

cDNA under the control of **CMV** promoter were cultured in IMDM-5% FBS and harvested at the concentration of 0.5 - 1 multiply 10 to power 6 cells/ml. The cells were centrifuged and resuspended in assay butter (20 mM HEPES, 140 mM sodium chloride, 1 mM calcium chloride, 5 mM magnesium chloride and with 0.2% bovine serum albumin) to a concentration of 5.6 multiply 10 to power 6 cells/ml. First cells (0.09 ml) was added to 8-assay plates containing **methiothepin** mesylate (a) (having a final concentration of 5 micro g/ml). 125I-Fractalkine (0.09 ml) diluted in assay butter was added, the plates sealed and incubated for 3 hours. The assay plates were harvested, presoaked in PEI solution. Scintillation fluid (35 micro l) was added to all wells, the plates were sealed and counted. Control wells containing diluent or excess fractalkine were used to calculate % of total inhibition for (a). The IC50 of (a) against fractalkine binding on US28-NSO cell was 0.3 micro M.

USE - For identifying compounds useful for blocking **CMV** dissemination in a host (preferably human); which are used for preventing the dissemination of **CMV** in a human; and reducing cell motility in a **CMV**-infected cell (claimed), particularly for treating immuno-compromized individuals such as AIDS patients, neonates or having transplant implantation; in acute and re-immerging infections such as in retinitis, encephalitis, pneumocystis and in other pathologies; and in a variety of inflammatory conditions including coronary artery occlusion following heart transplantation, artherectomy and restenosis following angioplasty.

ADVANTAGE - The compounds prevent the dissemination of **CMV** and reduce cell motility in a **CMV**-infected cell. By inhibiting the dissemination of the virus from the sites of primary or recurrent infection, the compounds can limit the viral spread to secondary organs and thus limit viral replication. Unlike current herpes antiviral agents, the compounds do not act at the stage of viral DNA replication and hence are less prone to problems with toxicity and the development of viral resistance.

Dwg.0/2

FS CPI EPI

FA AB; GI; DCN

MC CPI: B06-H; B11-C10; B14-A02B1; B14-C03; B14-F01; B14-N16

TECH UPTX: 20020516

TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Compounds: (a) is a compound of formula (I) (preferably a compound of formula (Ib)).

m = 0 - 3 (preferably 0);

n = 0 - 3 (preferably 1);

R1' = T1;

R2' = T1 (preferably halogen, 1-4C (halo)alkyl, 1-4C alkoxy or 1-4C alkylthio, especially halogen or 1-4C alkylthio); and

R3' = a substituent selected from 1-4C (halo)alkyl or 1-4C acyl.

TECHNOLOGY FOCUS - BIOLOGY - Preferred Components: The chemokine is fractalkine, MIP-1alpha, -1beta, MCP-1 or RANTES (preferably fractalkine). Preferred Method: The method involves specifically binding labeled fractalkine to the ligand binding domain of US28.

ABEX UPTX: 20020516

SPECIFIC COMPOUNDS - **Methiothepin** and **octoclothepin** are specifically claimed as (a).

ADMINISTRATION - The compounds are administered parenterally (e.g. intramuscularly or subcutaneously), orally (e.g. sublingually) or rectally. The dosage for parenteral administration is (0.01 - 250, preferably 0.5 - 30, more preferably 1 - 20, especially 1 - 10) mg/kg/day. The dosage for oral administration is (0.5 - 20, preferably 0.05 - 2, especially 0.05 - 0.2) mg/kg/day.

EXAMPLE - No relevant example given.

DEFINITIONS - Preferred Definitions:
X1, X3 and X4 and Y1 - Y4 = CH; and
R = substituted 6-membered heterocycle.

=> d all abeq tech abex tot l72

L72 ANSWER 1 OF 8 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN
AN 2003-851613 [79] WPIX
CR 2003-332863 [31]; 2003-342441 [32]; 2003-662906 [62]
DNC C2003-239899
TI Composition useful for treating **cytomegalovirus** or **cytomegalovirus**-related diseases e.g. atherosclerosis comprises arylamine derivatives and a carrier.
DC B03 B05
IN DAIRAGHI, D J; MCMASTER, B E; **PENFOLD, M; SCHALL, T J;** WRIGHT, J J
PA (CHEM-N) **CHEMOCENTRYX INC**
CYC 1
PI US 2003114423 A1 20030619 (200379)* 18p A61K031-675
ADT US 2003114423 A1 Provisional US 2001-316386P 20010830, US 2002-233336 20020829
PRAI US 2001-316386P 20010830; US 2002-233336 20020829
IC ICM A61K031-675
ICS A61K031-4178; A61K031-454; A61K031-4709; A61K031-496; A61K031-5377
AB US2003114423 A UPAB: 20031208
NOVELTY - A pharmaceutical composition (C1) comprises arylamine derivatives and a carrier.
DETAILED DESCRIPTION - A pharmaceutical composition comprises arylamine of formula Ar-L-N(R1)-R2 (I) and a carrier.
Ar = 5 - 14 membered heteroaryl group or 6-14C aryl (both optionally substituted);
q = 0 - 3;
R5 = halo, NO2, CN, R, OR, NR2, CO2R, C(O)R, OC(O)R, NRC(O)R or NRC(O)NR2;
R = H or 1-8C alkyl;
R3 and R4 = 1-4C alkyl;
L = linkage having 2 - 14 contiguous chain atoms selected from C, N, O, P and S (optionally mono- - tetra-substituted by T1);
R1 and R2 = 1-4C alkyl (optionally mono- - tetra-substituted by T1);
T1 = halo, OR', SR', S(O)pR' or CO2R';
R' = H or R3;
p = 1 or 2;
N(R1R2) and N(R3R4) = a ring selected from aziridine, azetidine, pyrrolidine, piperidine, imidazoline, piperazine or morpholine (all optionally mono- - tri-substituted by T2); and
T2 = 1-4C alkyl, phenyl, phenyl(1-4C)alkyl, hydroxy, hydroxy(1-4C)alkyl, 1-4C alkoxy(1-4C)alkyl or di(1-4C)alkylamino(1-4C)alkyl.
An INDEPENDENT CLAIM is included for arylamine of formula (Ia).
m and n = 1 or 2;
R'1 and R'2 = 1-4C alkyl (optionally substituted by OH or 1-4C alkoxy);
N(R'1R'2) = N(R1R2);
R'3 and R'4 = R3; and
N(R'3R'4) = Q1;
Q1 = aziridine, azetidine, pyrrolidine or piperidine (optionally mono- or di-substituted by 1-4C alkyl).
ACTIVITY - Virucide; Antiarteriosclerotic; Cardiovascular-Gen.
MECHANISM OF ACTION - Inhibitor of chemokine (preferably fractalkine, RANTES, MCP-3, MIP-1 alpha and MCP-1) binding to US28; **cytomegalovirus** (**CMV**) dissemination blocker.
CMV dissemination inhibiting activity of

1-diethylamino-3-(5-nitro-2-pyrrolidin-1-yl-phenoxy)-propan-2-ol (A) was determined by an assay providing an indication of fractalkine binding to US28. Human foreskin fibroblast (HFF) cell lines were transfected with US28cDNA. The cells were cultured in a buffer (containing IMDM-5% FBS), centrifuged and re-suspended in assay buffer. Aliquots of the cells were then contacted with (A) and labeled with fibroblasts. The assay mixture was incubated for 2 - 4 hours at 4 deg. C. Following the incubation the assay wells were harvested under vacuum, plates were sealed and the wells were counted. IC50 was determined which was less than 1 micro M.

USE - For treating **CMV** or **CMV**-related diseases (claimed) e.g. atherosclerosis or cardiovascular disease; to treat disease or provide medical prophylaxis to individuals who possess a compromised immune system or suffer immunosuppressed conditions e.g. prior to undergoing immunosuppressive therapy in connection with organ transplantation or anticancer chemotherapy.

ADVANTAGE - (I) inhibits chemokine binding to US28 on the surface of an infected cell or virion.

Dwg.0/0

FS CPI
FA AB; GI; DCN
MC CPI: B06-D01; B06-D02; B06-D03; B06-D05; B07-D01; B07-D03; B07-D05; B14-A02; B14-F01; B14-F02; B14-F07; B14-G02
ABEX UPTX: 20031208

ADMINISTRATION - (C1) is administered in a daily dosage of 2 - 2000 mg orally, parenterally (including intramuscularly, intravenously or subcutaneously) or topically. The oral dosage is 0.05 - 20 (preferably 0.05 - 2, especially 0.05 - 0.2) mg/kg of body weight per day. The parenteral dosage is 0.01 - 250 (preferably 0.5 - 30, especially 1 - 20) mg/kg/day.

EXAMPLE - No relevant example given.

DEFINITIONS - Preferred Definitions:

Ar = N(R3)(R4)-phenyl (substituted by (R5)q);
R1, R2, R'1 and R'2 = ethyl;
L = -NH-CH(CH3)CH2CH2CH2-, -CH2CH2-, -OCH2CH(OH)CH2- or -NHCH2CH2CH2-;
R5 = halo, NO2, CN, CO2R or C(O)R;
R = H or 1-4C alkyl;
N(R3R4) = pyrrolidine, piperidine or morpholine;
m and n = 1; and
N(R'3R'4) = a pyrrolidine ring.

L72 ANSWER 2 OF 8 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN
AN 2003-662906 [62] WPIX
CR 2003-332863 [31]; 2003-342441 [32]
DNC C2003-180024
TI Treatment of **cytomegalovirus** or its related diseases e.g. retinitis and encephalitis, involves use of bicyclic compounds..
DC B02
IN DAIRAGHI, D J; MCMASTER, B E; **PENFOLD, M; SCHALL, T J;** WRIGHT, J J
PA (CHEM-N) **CHEMOCENTRYX**
CYC 1
PI US 2003149055 A1 20030807 (200362)* 29p A61K031-506
ADT US 2003149055 A1 Provisional US 2001-316386P 20010830, US 2002-233326 20020829
PRAI US 2001-316386P 20010830; US 2002-233326 20020829
IC ICM A61K031-506
ICS A61K031-4439; A61K031-46; A61K031-4709
AB US2003149055 A UPAB: 20030928

NOVELTY - Treatment of **cytomegalovirus** or its related diseases involves administration of bicyclic compounds (I).

DETAILED DESCRIPTION - Treatment of **cytomegalovirus** or its related diseases involves administration of bicyclic compounds of formula

Ar-C(R2)(OR1)-Z (I).

Ar = optionally substituted 5-14 membered heteroaryl group having 1-5 heteroatoms;

R1 = optionally substituted (hetero)aryl(1-4C alkyl), -C(O)R11 or C(O)NR11R12;

R11 and R12 = (hetero)aryl, (hetero)aryl(1-4C alkyl), 4-8C cycloalkyl(1-4C alkyl) or hetero(4-8C cycloalkyl)(1-4C alkyl) (all optionally substituted);

R2 = H or 1-8C alkyl; and

Z = optionally substituted hetero(6-10C bicycloalkyl).

An INDEPENDENT CLAIM is also included for a pharmaceutical composition comprising (I) and a carrier.

ACTIVITY - Virucide; Ophthalmological; Neuroprotective; Antiinflammatory; Respiratory; Cardiant; Vasotropic.

MECHANISM OF ACTION - US28-Receptor-Binding-Chemokine-Inhibitor.

The efficacy of 3-nitro-benzoic acid quinolin-4-yl-(5-vinyl-1-azabicyclo(2.2.2)oct-2-yl)-methyl ester (A) to inhibit binding of fractalkine to US28 receptor was evaluated by radioligand binding assay. The target cells - US68 transfected murine cells (4 multiply 105 - 5 multiply 106 cells/ml) (0.09 ml) were added to assay plates containing (A) (0.02 ml) diluted in dimethylsulfoxide. 125I-fractalkine (approx. 50 micro M) was added to the assay plate and the plates were sealed. After incubation at 4 deg. C for 2-4 hours, the plates were harvested on a Packard vacuum cell harvester. Scintillation fluid was added to the wells, the plates were sealed and then counted in a Top count scintillation counter. (A) showed an IC50 value of less than 1 micro M.

USE - For inhibiting chemokine (e.g. fractalkine) to US28 on the surface of an infected cell or virion; for treating **cytomegalovirus** or its related diseases (claimed) (e.g. retinitis, encephalitis, pneumocystis, coronary artery occlusion following heart transplant and atherectomy, and restenosis following angioplasty).

ADVANTAGE - The bicyclic compounds are potent inhibitors of US28 receptor.

Dwg.0/0

FS CPI

FA AB; GI; DCN

MC CPI: B07-H; B14-F01; B14-F02; B14-L06; B14-N03; B14-N16

TECH UPTX: 20030928

TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preferred Compound: The bicyclic compound is also of formula (Ia).

n = 0 - 3;

R13 = halo, NO2, CN, R, OR, NR2, CO2R, C(O)R, OC(O)R, NRC(O)R or NRC(O)NR2;

R = H or 1-8C alkyl;

R14 = H or optionally substituted 1-8C alkyl (preferably unsaturated 2-8C alkyl, particularly vinyl).

ABEX UPTX: 20030928

SPECIFIC COMPOUNDS - 7 Compounds are specifically claimed as (I), e.g. 3-nitro-benzoic acid quinolin-4-yl-(5-vinyl-1-azabicyclo(2.2.2)oct-2-yl)-methyl ester (Ib).

ADMINISTRATION - The dosage is 2-2000 mg/day. The dosage for oral administration is 0.05-20 (preferably 0.05-2, especially 0.05-0.2) mg/kg/day, and for parenteral (e.g. intramuscular, intravenous, or subcutaneous) administration is 0.01-250 (preferably 1-100, especially 0.5-30, particularly 1-20) mg/kg/day. Administration is also rectally, topically or by intraocular implant.

EXAMPLE - No relevant example given.

DEFINITIONS - Preferred Definitions:

Ar = quinoline, isoquinoline, pyridine or pyrimidine;

R1 = C(O)R11 or C(O)NR11R12;

R2 = H; and
Z = 1-azabicyclo(2.2.2)octane, 2-azabicyclo(2.2.2)octane, 1-azabicyclo(3.2.2)nonane, 2-azabicyclo(3.2.2)nonane, 1-azabicyclo(2.2.1)heptane or 2-azabicyclo(2.2.1)heptane.

L72 ANSWER 3 OF 8 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN
AN 2003-342441 [32] WPIX
CR 2003-332863 [31]; 2003-662906 [62]; 2003-851613 [79]
DNC C2003-089814
TI Treatment of **cytomegalovirus** infections or related diseases, using O-substituted 1-heteroaryl-1-heterobicycloalkyl-alkanol compounds, preferably cinchonidine benzoate derivatives.
DC B02
IN DAIRAGHI, D J; MCMASTER, B E; **PENFOLD, M; SCHALL, T J;** WRIGHT, J J
PA (CHEM-N) **CHEMOCENTRYX INC**
CYC 101
PI WO 2003018549 A2 20030306 (200332)* EN 38p C07D000-00
RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SK SL SZ TR TZ UG ZM ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW
ADT WO 2003018549 A2 WO 2002-US28007 20020829
PRAI US 2001-316386P 20010830
IC ICM C07D000-00
AB WO2003018549 A UPAB: 20031208
NOVELTY - Treatment of **cytomegalovirus** (**CMV**) diseases or **CMV**-related diseases involves administration of an O-substituted 1-heteroaryl-1-heterobicycloalkyl-alkanol derivative (I).
DETAILED DESCRIPTION - Treatment of **CMV** diseases or **CMV**-related diseases involves administration of a heterobicyclic compound of formula (I).
Ar = optionally substituted (os) 5-14 membered heteroaryl;
R1 = os aryl-(1-4C) alkyl, heteroaryl-(1-4C) alkyl, COR11 or CONR11R12;
R11, R12 = os aryl, os aryl-(1-4C) alkyl, aryl-(1-4C) alkyl, os (4-8C) cycloalkyl-(1-4C) alkyl, os heteroaryl, os heteroaryl-(1-4C) alkyl or os (4-8C) heterocycloalkyl-(1-4C) alkyl;
R2 = H or 1-8C alkyl;
Z' = os 6-10C heterobicycloalkyl.
An INDEPENDENT CLAIM is also included for a pharmaceutical composition comprising a compound (I) and a carrier.
ACTIVITY - Virucide; Ophthalmological; Neuroprotective; Antiinflammatory; Antiarteriosclerotic; Cardiant. 2-Chlorobenzoic acid cinchonidine ester (Ia) had an IC50 less than 1 micro M against rhesus **CMV**.
MECHANISM OF ACTION - Inhibition of chemokine binding to US28 on infected cell or virion surface.
(Ia) had an IC50 1-10 micro M for inhibition of hUS28 binding.
USE - (I) inhibit the binding of chemokines (especially fractalkine) to US28 on the surface of infected cells or virions (claimed), and are thus useful for inhibiting viral dissemination during acute or re-emerging **CMV** infection. (I) are typically used for the treatment of **CMV** infections in immunocompromized patients (e.g. AIDS patients, neonates or patients undergoing immunosuppressive therapy in connection with organ transplantation or anticancer chemotherapy); or for treating **CMV**-related diseases (e.g. retinitis, encephalitis, pneumocystitis, atherosclerosis or cardiovascular disease) in non-immunocompromized patients.
ADVANTAGE - (I) are small molecule inhibitors of the **CMV**

US28 receptor.
Dwg.0/0

FS CPI
FA AB; GI; DCN
MC CPI: B04-A02; B07-H; B14-A02; B14-L06
TECH UPTX: 20030522
TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Compounds: (I) are cinchonine (or analog) benzoate ester derivatives of formula (I').
n = 0-3;
R13 = halo, NO2, CN, R, OR, N(R)2, COOR, OCOR, NRCOR or NRCON(R)2;
R = H or 1-8C alkyl;
R14 = H or os 1-8C alkyl (preferably unsaturated 2-8C alkyl, especially vinyl).

TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preferred Process: (I) are typically prepared by reaction of an aldehyde or ketone of formula ArCOR2 with a Grignard reagent of formula Z'-Mg-Br, followed by O-alkylation or O-acylation of the obtained alcohol.
ABEX UPTX: 20030522
SPECIFIC COMPOUNDS - 7 Compounds (I) are specified in the claims, e.g. 2-chlorobenzoic acid cinchonidine ester (Ia).

ADMINISTRATION - Administration is oral, parenteral or topical at a daily dose of 2-2000 mg, preferably 0.05-20, especially 0.05-0.2 mg/kg/day orally. (I) are optionally used in combination with other drugs, such as other antiviral agents (e.g. ganciclovir), anti-HIV agents (e.g. AZT) or immunosuppressants (e.g. cyclosporin).
DEFINITIONS - Preferred Definitions:
Ar = quinoline, isoquinoline, pyridine or pyrimidine;
Z' = 1- or 2-azabicyclo (2.2.2)-octane, 1- or 2-azabicyclo (3.2.2)-nonane or 1- or 2-azabicyclo (2.2.1)-octane;
R1 = COR11 or CONR11R12;
R2 = H.

L72 ANSWER 4 OF 8 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN
AN 2003-332863 [31] WPIX
CR 2003-342441 [32]; 2003-662906 [62]; 2003-851613 [79]
DNC C2003-086287
TI Treatment of **cytomegalovirus** or related diseases comprising administration of arylamines.
DC B03 B05
IN DAIRAGHI, D J; MCMASTER, B E; **PENFOLD, M; SCHALL, T J;** WRIGHT, J J
PA (CHEM-N) **CHEMOCENTRYX INC**
CYC 101
PI WO 2003020029 A1 20030313 (200331)* EN 39p A01N033-02
RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SK SL SZ TR TZ UG ZM ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW
ADT WO 2003020029 A1 WO 2002-US27812 20020829
PRAI US 2001-316386P 20010830
IC ICM A01N033-02
ICS A01N031-14; A01N033-18; A01N033-24; A61K031-075; A61K031-135
AB WO2003020029 A UPAB: 20031208
NOVELTY - **Cytomegalovirus** (**CMV**) or **CMV**-related diseases are treated by administering arylamines (I).
DETAILED DESCRIPTION - **Cytomegalovirus** (**CMV**) or **CMV**-related diseases are treated by administering arylamines of formula Ar-L-N-R1R2 (I).

Ar = 5 - 14 membered heteroaryl or 6-14C aryl (both optionally substituted);

L = optionally substituted 2 - 14 contiguous chain atom containing C, N, O, P or S (optionally substituted by T1;

R1, R2 = 1-4C alkyl (optionally substituted by T1); or

NR1R2 = aziridine, azetidine, pyrrolidine, piperidine, imidazoline, piperazine or morpholine (all optionally mono- to tri-substituted by 1-4C alkyl, phenyl, phenyl(1-4C)alkyl, OH, hydroxy(1-4C)alkyl, 1-4C alkoxy(1-4C)alkyl or di(1-4C)alkylamino(1-4C)alkyl;

T1 = halo, OR', SR', S(O)pR' or CO2R';

R' = H or 1-4C alkyl; and

p = 1 or 2.

An INDEPENDENT CLAIM is also included for an arylamine of formula (Ia).

m, n = 1 or 2;

R6, R7 = 1-4C alkyl (optionally substituted by OH or 1-4C alkoxy); or

NR6R7 = NR1R2; and

R3, R4 = 1-4C alkyl; or

NR3R4 = aziridine, azetidine, pyrrolidine or piperidine (optionally mono- - di-substituted by 1-4C alkyl).

ACTIVITY - Virucide.

MECHANISM OF ACTION - Chemokine Binding Inhibitor.

In radioligand binding assays on rhesus dermal fibroblast cells (4 multiply 105 - 5 multiply 106) infected with **cytomegalovirus** (**CMV**) (I) was found to have an IC50 value of less than 1 micro M for binding of labeled fractalkine to the US28 surface receptor.

USE - (I) Are used for treating **cytomegalovirus** (**CMV**) or **CMV** related diseases (claimed) such as atherosclerosis or cardiovascular diseases. They are useful for patients with a compromised immune system or those who are expected to suffer immunosuppressed condition (such as those about to undergo immunosuppressive therapy in connection with organ transplant or anticancer chemotherapy). They inhibit chemokine (particularly fractalkine) binding to US28 on the surface of infected cells or virions.

ADVANTAGE - (I) Are in the from of pro-drug which can be metabolically or chemically converted into the active drug by the recipient host, which rely on hydrolytic cleavage or oxidative activation of the pro-drug. The composition containing (I) can be combined with other pharmaceutical agents like antiviral agents and these compositions show high efficacy.

Dwg.0/0

FS CPI

FA AB; GI; DCN

MC CPI: B05-B01E; B05-B01F; B07-H; B10-B02A; B10-B02B; B10-B04B; B14-A02; B14-A02A3; B14-F02; B14-F07; B14-G01; B14-G02; B14-G02C; B14-G03; B14-L01

ABEX UPTX: 20030516

SPECIFIC COMPOUNDS - 1 Compound (I) is specifically disclosed, i.e. (S)-1-((2-pyrrolidino-5-nitro)phenyloxy)-3-(N,N-diethylamino)propan-2-ol (Ib).

ADMINISTRATION - The dosage is 2 - 2000 mg/kg and is administered rectally, topically, intraocularly, or parenterally (including intramuscularly, intravenously or subcutaneously). The dosage for oral administration is 0.05 - 20 (preferably 0.05 - 0.2) mg/kg.

EXAMPLE - N-(2-hydroxy-4-nitrophenyl)pyrrolidine (3 g), (S)-(+)-epichlorohydrin (1.4 g) and dry potassium carbonate (2.6 g) in dry acetonitrile (40 ml) were stirred at 60 degrees C overnight. Water (100 ml) was added and the mixture was worked up to give a crude epoxide (3 g, 78%).

The crude epoxide (100 mg) and diethylamine (3 ml) were stirred at room temperature overnight. The solution was concentrated, and the yellow product was purified by column chromatography (eluant was 0.2% methanol in

chloroform) to give (S)-1-((2-pyrrolidino-5-nitro)phenyloxy)-3-(N,N-diethylamino)propan-2-ol (60 mg, 47%).

DEFINITIONS - Preferred Definitions:
Ar = phenyl (substituted by NR3R4 and optionally mono- - tri-substituted by R5);
L = -NHCH(CH3)CH2CH2CH2-, -CH2CH2-, -OCH2CH(OH)CH2- or -NHCH2CH2CH2-;
R1, R2, R6, R7 = ethyl;
R5 = halo, NO2, CN, CO2R or C(O)R;
R = H or 1-4C alkyl; and
NR3R4 = pyrrolidine, piperidine or morpholine.

L72 ANSWER 5 OF 8 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN
AN 2002-643385 [69] WPIX
DNC C2004-014231
TI Recombinant **cytomegalovirus** with a **CMV** genome with a first heterologous nucleotide sequence encoding a heterologous chemokine element, useful for inducing an immune response, and in therapeutic or prophylactic treatments.
DC B04 C06 D16
IN **PENFOLD, M E T; SCHALL, T J**
PA (CHEM-N) **CHEMOCENTRYX INC**
CYC 101
PI WO 2002062296 A2 20020815 (200269)* EN 74p A61K000-00
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZM ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG US UZ VN YU ZA ZM ZW
US 2002176870 A1 20021128 (200281) A61K039-245
EP 1364037 A2 20031126 (200380) EN C12N015-83
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI TR
ADT WO 2002062296 A2 WO 2002-US3228 20020201; US 2002176870 A1 Provisional US 2001-265925P 20010202, US 2002-61943 20020201; EP 1364037 A2 EP 2002-707692 20020201, WO 2002-US3228 20020201
FDT EP 1364037 A2 Based on WO 2002062296
PRAI US 2001-265925P 20010202; US 2002-61943 20020201
IC ICM A61K000-00; A61K039-245; C12N015-83
ICS A61K039-25; C12N007-00
AB WO 200262296 A UPAB: 20040115
NOVELTY - A new recombinant **cytomegalovirus** (**CMV**) (I) comprising a **CMV** genome with a first heterologous nucleotide sequence encoding a heterologous chemokine element, and a second heterologous nucleotide sequence encoding an immunogenic polypeptide, is new.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for:
(1) a recombinant **CMV** comprising a genome with a heterologous nucleotide sequence encoding a heterologous chemokine or ligand, or an immunogenic polypeptide;
(2) inducing (M1) an immune response in a host comprising administering a composition of (I);
(3) therapeutic or prophylactic treatment (M2) comprising administering a composition of (I) to an animal, where the immunogenic polypeptide comprises an antigen correlated with a disease or infection which the animal has or is susceptible to obtaining, and where the administration induces an immune response in the animal; and
(4) preparing (M3) (I).
ACTIVITY - Virucide.
No suitable data given.
MECHANISM OF ACTION - Gene therapy; Vaccine.

USE - (I) are useful for inducing an immune response in a host and in treatment methods, either therapeutically or prophylactically (claimed). Dwg.0/8

FS CPI

FA AB; DCN

MC CPI: B04-B04C; B04-E03F; **B04-F11**; B14-A02; B14-G01; B14-S03; B14-S11; C04-B04C; C04-E03F; **C04-F11**; C14-A02; C14-G01; C14-S03; C14-S11; **D05-H06A**; D05-H12A

TECH UPTX: 20030513

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred **Cytomegalovirus**:

The **CMV** genome in (I) is encapsulated in infectious form as a virion, and attenuated to reduce virulency in a host. The viral dissemination gene is disabled, and is a gene encoding a viral chemokine element or a viral immune-modulatory gene. The gene encoding the viral chemokine element is selected from US28, US27, UL33, UL78, UL146, UL147, MCK-1 and MCK-2, or their homolog. The viral immune-modulatory gene is selected from UL111A, US3, US6, US11, US2, UL83, UL18, UL40, m144, m152, m04, m06 and m138, or their homolog. The host is selected from a non-human primate or commercial livestock. The mammal is a rhesus monkey or a mouse. The heterologous chemokine element is endogenous to the host, and is a chemokine ligand or receptor. The **CMV** genome is attenuated to reduce virulency in a mammal and the heterologous chemokine element is selected from MIP3alpha, SLC, MDC, MC10, MIP1beta, ELC and CCR7, or their homolog. The immunogenic polypeptide comprises an antigen from a pathogenic organism or a tumor antigen. The pathogenic organism is a bacterium, a virus or a parasite. The immunogenic polypeptide further comprises a fragment of a polypeptide from organisms selected from Bacillus anthracis, Dengue, Yersinia pestis, Ebola, Marburg, Lassa, Venezuelan Equine Encephalitis or Eastern Equine Encephalitis. The immunogenic polypeptide preferably comprises a tumor antigen, and is selected from antigens associated with breast cancers, lung cancers, thyroid carcinomas, squamous cell carcinomas or renal cell carcinomas. The first and second heterologous nucleotide sequence are operably linked to a or different promoters that is operative in the host. The construct is formulated as a composition, the composition comprising the construct and an adjuvant, carrier, diluent or excipient. (I) further comprises:

(a) the immunogenic polypeptide comprising an antigen from an organism that is pathogenic in humans or a human tumor antigen;

(b) a viral chemokine element or a viral immune-modulatory gene is disabled, the viral chemokine element selected from US28, U827, UL33, UL78, UL146 and UL147 and the viral immune-modulatory gene selected from UL111A, US3, US6, US11, US2, UL83, UL18 and UL40; and

(c) the heterologous chemokine element is selected from MIP3alpha, SLC, MDC, MC10, MIP1beta, ELC and CCR7, or their homolog.

The **CMV** genome in the recombinant virus is attenuated by virtue of a disabled viral dissemination gene and/or a viral immune-modulatory gene, and is attenuated to reduce virulency in a host and encapsulated in infectious form. The immunogenic polypeptide comprises an antigen from an organism that is pathogenic in a host or a tumor antigen.

Preferred Method: The **CMV** genome in (M1) is attenuated to reduce virulency in the host, and is disabled. The viral dissemination gene is a gene encoding a viral chemokine element or a viral immune-modulatory gene. The gene encoding the viral chemokine element is selected from US28, US27, UL33, UL78, UL146, UL147, MCK-1 and MCK-2, or their homolog. The viral immune-modulatory gene is selected from UL111A, US3, US6, US11, US2, UL83, UL18, UL40, m144, m152, m04, m06 and m138, or a homolog. The heterologous chemokine element is endogenous to the host. The heterologous chemokine element is a chemokine ligand or receptor. The host is a mammal and the heterologous chemokine element is selected from MIP3alpha, SLC, MDC, MC10, MIP1beta, ELC and CCR7, or their homolog. The pathogenic organism is a bacterium, a virus or a parasite. (M1) further comprises:

(a) the host is a human;

(b) a viral chemokine element or a viral immune-modulatory gene is

disabled, the viral chemokine element selected from US28, US27, UL33, UL78, UL146, and UL147 and the viral immune-modulatory gene selected from UL111A, US3, US6, US11, US2, UL83, UL18 and UL40;
(c) the heterologous chemokine element is selected from MIP3alpha, SLC, MDC, MC10, MIP1beta, ELC and CCR7, or their homolog; and
(d) the immunogenic polypeptide comprises an antigen from an organism that is pathogenic in humans or a human tumor antigen.
The method alternatively comprises:
(a) the host is a rhesus monkey;
(b) a viral chemokine element or a viral immune-modulatory gene is disabled, the viral chemokine element selected from rhUS28.1, rhUS28.2, rhUS28.3, rhUS28.4, rhUS28.5, rhUL33 and rhUL78 and the viral immune-modulatory gene selected from rhUL111A, US3, US6, US11, US2, UL83 and UL40;
(c) the heterologous chemokine element is selected from MIP3alpha, SLC, MDC, MC10, MIP1beta, ELC and CCR7, or their homolog; and
(d) the immunogenic polypeptide comprises an antigen from a pathogenic organism or a tumor antigen.
The method further comprises:
(a) the host is a mouse;
(b) a viral chemokine element or a viral immune-modulatory gene is disabled, the viral chemokine element selected from MUL78, MCK-1 and MCK-2 and the viral immune-modulatory gene selected from m144, m152, m04, m06, m138;
(c) the heterologous chemokine element is selected from MIP3alpha, SLC, MDC, MC10, MIP1beta, ELC, CCR7 or their homolog;
(d) the immunogenic polypeptide comprises an antigen from a pathogenic organism or a tumor antigen.
The CMV genome in (M2) is attenuated by virtue of a disabled viral dissemination gene. The viral dissemination gene is a gene encoding a viral chemokine element or a viral immune-modulatory gene. The gene encoding the viral chemokine element is selected from US28, US27, UL33, UL78, UL146, UL147, MCK-1 and MCK-2, or their homolog. The viral immune-modulatory gene is selected from UL111A, US3, US6, US11, US2, UL83, UL18, UL40, m144, m152, m04, m06 and m138, or a homolog. The animal is a mammal. The animal is selected from a human, a non-human primate and commercial livestock. The mammal is from a non-human primate and a mouse.
The method further comprises:
(a) the host is a human;
(b) a viral chemokine element or a viral immune-modulatory gene is disabled, the viral chemokine element selected from US28, US27, UL33, UL78, UL146, and UL147 and the viral immune-modulatory gene selected from UL111A, US3, US6, US11, US2, UL83, UL18 and UL40;
(c) the heterologous chemokine element is selected from MIP3alpha, SLC, MDC, MC10, MIP1beta, ELC and CCR7, or their homolog; and
(d) the immunogenic polypeptide comprises an antigen from an organism that is pathogenic in humans or a human tumor antigen.
The method alternatively comprises:
(a) the host is a rhesus monkey;
(b) a viral chemokine element or a viral immune-modulatory gene is disabled, the viral chemokine element selected from rhUS28.1, rhUS28.2, rhUS28.3, rhUS28.4, rhUS28.5, rhUL33 and rhUL78 and the viral immune-modulatory gene selected from rhUL111A, US3, US6, US11, US2, UL83 and UL40;
(c) the heterologous chemokine element is selected from MIP3alpha, SLC, MDC, MC10, MIP1beta, ELC and CCR7, or their homolog; and
(d) the immunogenic polypeptide comprises an antigen from a pathogenic organism or a tumor antigen.
The method further comprises:
(a) the host is a mouse;
(b) a viral chemokine element or a viral immune-modulatory gene is disabled, the viral chemokine element selected from MUL78, MCK-1 and MCK-2 and the viral immune-modulatory gene selected from m144, m152, m04, m06,

m138;
(c) the heterologous chemokine element is selected from MIP3alpha, SLC, MDC, MC10, MIP1beta, ELC, CCR7 or their homolog;
(d) the immunogenic polypeptide comprises an antigen from a pathogenic organism or a tumor antigen.
(M3) further comprises attenuating the **CMV** genome to reduce virulency in a host. The attenuation comprises disabling a viral dissemination gene. The viral dissemination gene is a gene encoding a viral chemokine element or a viral immune-modulatory gene. The gene encoding the viral chemokine element is selected from US28, US27, UL33, UL78, ULI46, UL147, MCK-1 and MCK-2, or their homolog. The viral immune-modulatory gene is selected from UL111A, US3, US6, US11, US2, UL83, UL18, UL40, m144, m152, m04, m06 and m138, or their homolog. The host is selected from a human, a non-human primate and commercial livestock. The mammal is selected from the group consisting of a rhesus monkey and a mouse. The heterologous chemokine element is endogenous to the host, and is a chemokine ligand or receptor. The heterologous chemokine element is selected from MIP3alpha, SLC, MDC, MC10, MIP1beta, ELC and CCR7, or their homolog. The immunogenic polypeptide comprises an antigen from a pathogenic organism or a tumor antigen. The pathogenic organism is a bacterium, a virus or a parasite. The method further comprises inserting at least one promoter that is operative in the host into the **CMV** genome such that the at least one promoter is operably linked to the first and second heterologous nucleotide sequence. The method alternatively comprises inserting at least two promoters that are operative in the host into the **CMV** genome such that the first and second heterologous nucleotide sequence are operably linked to different promoters. The method further comprises combining (I) with a carrier, diluent or excipient.

ABEX UPTX: 20030513
ADMINISTRATION - The vaccine preparations dose are from 10 to 107 pfu per dose, preferably 103-106. Routes of administration include intradermal, subcutaneous, oral, intramuscular, intraperitoneal and transdermal.

EXAMPLE - Experimental protocols are described but no results are given.

L72 ANSWER 6 OF 8 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN
AN 2002-426421 [45] WPIX
DNC C2002-120897
TI Inhibiting proliferation of peripheral blood mononuclear cells and reducing cytokine production of monocytes using rhesus or human **cytomegalovirus** interleukin-10, for treating e.g. immune disorders.
DC B04
IN **PENFOLD, M; SCHALL, T J;** SPENCER, J; PENFORD, M
PA (CHEM-N) **CHEMOCENTRYX INC**
CYC 97
PI WO 2002032457 A1 20020425 (200245)* EN 69p A61K045-00
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW
AU 2001080911 A 20020429 (200255) A61K045-00
US 2002197234 A1 20021226 (200304) A61K038-20
EP 1307228 A1 20030507 (200332) EN A61K045-00
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI TR
ADT WO 2002032457 A1 WO 2001-US23942 20010730; AU 2001080911 A AU 2001-80911 20010730; US 2002197234 A1 Provisional US 2000-221831P 20000728, US 2001-919224 20010730; EP 1307228 A1 EP 2001-959344 20010730, WO 2001-US23942 20010730
FDT AU 2001080911 A Based on WO 2002032457; EP 1307228 A1 Based on WO

2002032457
PRAI US 2000-221831P 20000728; US 2001-919224 20010730
IC ICM A61K038-20; A61K045-00
ICS A01N037-18; A61K038-28; A61K039-12; C07K001-00; C12N005-08
AB WO 200232457 A UPAB: 20020717
NOVELTY - Inhibition of proliferation of peripheral blood mononuclear cells (PBMCs) and reduction of cytokine production of monocytes involves contacting the cells in vitro with rhesus or human **cytomegalovirus** interleukin (**CMV** IL)-10.

ACTIVITY - Immunosuppressive; Antiinflammatory; Vasotropic; Antipsoriatic; Ophthalmological; Dermatological; Neuroprotective; Antirheumatic; Antiarthritic; Antiulcer; Antithyroid; Thyromimetic; Antidiabetic; Antiallergic; Asthmatic; Virucide; Hepatotropic; Respiratory-Gen.; Cytostatic; and Antibacterial.

MECHANISM OF ACTION - PBMCs proliferation and cytokine production inhibitor.

USE - For inhibiting the proliferation of PBMCs and reducing the cytokine production of monocytes, for preventing or treating immune disorders (preferably in kidney transplant patients) (e.g. graft versus host disease, autoimmune disease, inflammatory response (preferably chronic inflammatory response e.g. rheumatoid arthritis, inflammatory bowel disease, Crohn's disease, ulcerative colitis, Grave's disease, Hashimoto's thyroiditis, scleroderma, insulin-dependent diabetes mellitus, allergic response and asthma), pathologic delayed type hypersensitivity response, endotoxin-induced toxic shock (toxic shock syndrome), granulomatis disease, psoriasis, uveitis, systemic lupus erythematous, multiple sclerosis, contact-dermatitis, leukemia and type TH1 immune response to transplanted graft of organs (e.g. cornea, lung, heart, liver, bone marrow, kidney, pancreas, blood, and skin)), respiratory viral infection, for ameliorating symptoms of hepatitis, for ameliorating liver damage, liver disease or liver fibrosis and for reducing an in vivo inflammatory response with substantially elevated levels of interleukin (IL)-1 alpha , GM-CSF, IFN- gamma or (TNF)- alpha (all claimed). Also for treating cytokine-mediated diseases including endotoxin-induced septic shock (bacterial septic shock), cell mediated cytotoxicity immune disorders, hypersensitivity immune disorders, chronic immune disorders, graft rejection and cancer.

ADVANTAGE - The treatment of monocytes with **CMV** IL-10 reduces cytokine production, monocyte surface expression of classical class I major histocompatibility complex (MHC) and class II MHC molecules and increases monocyte surface expression of the nonclassical class I MHC molecule, HLA-G which is beneficial in the treatment of various diseases.
Dwg.0/12
FS CPI
FA AB; DCN
MC CPI: B04-H02L; B14-A02; B14-C03; B14-C06; B14-E08; B14-E10C; B14-G02A; B14-G02C; B14-G02D; B14-H01; B14-K01A; B14-N03; B14-N11; B14-N12; B14-N17; B14-N17C; B14-S01; B14-S04; B14-S06
TECH UPTX: 20020717
TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Method: The method further involves adding an agent that induces the PBMCs to proliferate. The levels of interferon (IFN)-gamma and tumor necrosis factor- (TNF)-alpha secreted by the PBMCs and the monocytes and the levels of GM-CSF, IL-1alpha and IL-6 secreted by the monocytes are reduced in response to the contacting step. The proliferation level, the secretion of IFN-gamma, TNF-alpha, GM-CSF, IL-1alpha or IL-6 and the cytokine levels are monitored to determine a reduction in their levels.
Preferred Materials: The rhesus or human **CMV** IL-10 is a component of a composition further comprising a carrier. The composition is sterile, substantially isotonic and prepared under GMP conditions.
ABEX UPTX: 20020717
ADMINISTRATION - The dosage of purified human **CMV** IL-10 is 100 ng/ml, 1 ng/ml, 10 pg/ml, 100 pg/ml, 1 pg/ml or 100 ng/ml - 1 pg/ml.

Administration is oral, buccal, rectal, parenteral, intraperitoneal, intradermal, transdermal, intratracheal, intravenous, intramuscular, subcutaneous, or by inhalation in a local or systemic manner or in a depot or sustained release formulation.

EXAMPLE - Peripheral blood mononuclear cells (PBMCs) from nine human donors were tested for effects on proliferation in the presence of rhesus **cytomegalovirus** interleukin (**CMV** IL)-10, recombinant hIL-10 (1 mug/ml) conditioned media or mock conditioned media and PBMC proliferation was measured by using (3H)TdR incorporation assays. The % inhibition was 57 - 91%. Human PBMC proliferation for four donors inhibited in the presence of hIL-10 (1 mug/ml) was 16 - 81% while four other donors showed enhanced proliferation of 24 - 194% and one donor showed modest enhancement. The mean % change in proliferation with **CMV** IL-10 and IL-10 was -50 to -100 and 0 - 50 respectively. The experiment was also conducted similarly with human **CMV** IL-10 and IL-10 with almost the same results for the % change in proliferation.

L72 ANSWER 7 OF 8 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN
AN 2002-351718 [38] WPIX
CR 2002-269444 [31]; 2002-304220 [34]
DNN N2002-276368 DNC C2002-099891
TI Isolated or recombinant homologs of US28 proteins and nucleic acids encoding the proteins, for use in vaccine compositions for treating an animal infected with, or at risk of infection by, **cytomegalovirus**.
DC B02 B03 B04 D16 K08 S03
IN DAIRAGHI, D J; MCMASTER, B E; **SCHALL, T J; PENFOLD, M E T; PENFOLD, M**
PA (CHEM-N) **CHEMOCENTRYX INC**; (PENF-I) PENFOLD M E T; (SCHA-I) SCHALL T J
CYC 98
PI WO 2002018954 A2 20020307 (200238)* EN 95p G01N033-569
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PH PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 2001088682 A 20020313 (200249) G01N033-569
US 2002127544 A1 20020912 (200262) C12Q001-70
US 2003175681 A1 20030918 (200362) C12Q001-70
EP 1350113 A2 20031008 (200370) EN G01N033-569
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI TR
ADT WO 2002018954 A2 WO 2001-US27392 20010830; AU 2001088682 A AU 2001-88682 20010830; US 2002127544 A1 Provisional US 2000-228974P 20000830, Provisional US 2000-229191P 20000830, Provisional US 2000-229365P 20000830, US 2001-944163 20010830; US 2003175681 A1 Provisional US 2000-229365P 20000830, US 2001-944049 20010830; EP 1350113 A2 EP 2001-968433 20010830, WO 2001-US27392 20010830
FDT AU 2001088682 A Based on WO 2002018954; EP 1350113 A2 Based on WO 2002018954
PRAI US 2000-229365P 20000830; US 2000-228974P 20000830; US 2000-229191P 20000830; US 2001-944163 20010830; US 2001-944049 20010830
IC ICM C12Q001-70; G01N033-569
ICS A61K031-473; A61K031-498; A61K031-519; A61K039-245; A61K039-255; A61K039-265; A61K039-27; A61K039-395; A61K048-00; A61P031-12; C07K014-00; C12N005-00; C12N015-00; C12P019-34; C12P021-06
AB WO 200218954 A UPAB: 20031030
NOVELTY - An isolated or recombinant homolog of US28 protein (I) which binds a chemokine (encoded by an open reading frame in the unique short (US) region in human **cytomegalovirus** (**CMV**) genome),

having at least 75% identity to a sequence (S1) fully defined in the specification, over a region of at least 40 amino acids in length, or a protein comprising at least 12 amino acids of S1, is new.

DETAILED DESCRIPTION - S1 comprises a sequence of 344, 339, 340, 328, 485, 401, 365 or 423 amino acids fully defined in the specification (amino acid sequences of rhesus monkey proteins RhUS28.1, RhUS28.2, RhUS28.3. RhUS28.4, RhUS28.5, RhUL78 (encoded by an open reading frame 78 in the unique long (UL) region of **CMV** genome), RhUL33 and RhUL33 spliced, respectively).

INDEPENDENT CLAIMS are also included for the following:

(1) an isolated, purified or recombinant nucleic acid (II) encoding (I) (US28 homolog);

(2) a vector comprising (II);

(3) a cell comprising (II);

(4) a vaccine (III) comprising an immunogenic **CMV** polypeptide encoded by at least a region of **CMV** genome in which the polynucleotide sequence encoding US28 or its homolog has been inactivated;

(5) identifying (M1) an agent that reduces **CMV** dissemination in an animal, by determining whether the agent (A) inhibits the expression or activity of US28 or US28 homolog, or fragment or variant of US28 or US28 homolog; and

(6) treating (M2) an animal infected with **CMV** or at risk of infection by **CMV**, by administering (A) to the animal.

ACTIVITY - Virucide; neuroprotective; antiinflammatory; ophthalmological.

MECHANISM OF ACTION - Inhibitor of **CMV** dissemination; inhibitor of binding of chemokine to US28; vaccine (claimed).

No suitable data given.

USE - (III) is useful for treating an animal infected with **cytomegalovirus** or at a risk of infection by **CMV**. (III) is also useful for inducing a therapeutic or protective immune response in a patient and in methods for treating diseases including retinitis, encephalitis and pneumocystis caused by **CMV** infection.

Dwg.0/7

FS CPI EPI

FA AB; DCN

MC CPI: B04-B04B1; B04-B04D5; B04-B04G; B04-C01G; B04-E02F; B04-E03F; B04-E05; B04-E06; B04-E07; B04-E08; B04-F0100E; B04-G08; B04-N02A; B04-N02A0E; B11-C07A; B11-C08E5; B11-C09; B12-K04A4; B14-A02A3; B14-C03; B14-N03; B14-N16; B14-S11A; **D05-H06A**; D05-H07; D05-H12A; D05-H12D1; D05-H12D2; D05-H12D4; D05-H12E; D05-H14B2; D05-H17A6; D05-H18B

EPI: S03-E14H; S03-E14H4

TECH UPTX: 20020618

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preparation: (I) is produced by standard recombinant techniques.

Preferred Method: M1 involves contacting a chemokine with US28, US28 homolog, its fragment or variant, or a cell expressing the above said compounds, in the presence of (A) and determining whether (A) inhibits the binding between the chemokine and US28, its homolog, fragment or variant. The (A) is an antibody that specifically binds to (I), or a small molecule. The cell is infected with **CMV** or transfected with a heterologous nucleic acid encoding US28, its homolog, fragment or variant. The protein comprises at least 10 contiguous amino acids of S1 and binds to the chemokine. The method further involves administering (A) to a non-human animal infected with **CMV** and determining whether (A) inhibits the dissemination of **CMV** from a primary site of infection in non-human animal such as primate e.g. rhesus monkey. The **CMV** is rhCMV. The method further involves determining whether viral titer in a saliva, urine or blood sample obtained from the non-human animal is detectably less than viral titer in a corresponding sample obtained from a control animal. The method further involves obtaining a

peripheral blood sample from a non-human animal, amplifying a region of **CMV** which is present in the sample with a set of primers that specifically hybridize to a set of **CMV** genome to form an amplified product, and detecting the amplified product. The method involves obtaining and staining a tissue sample of a non-human animal with an antibody that specifically binds to **CMV**. Alternately, activated T cells and/or memory cells in a peripheral blood sample taken from the non-human animal are detected. In M2, (A) interferes with the expression of a target nucleic acid encoding (I) in cells of the animal. The interference is achieved by administering an antisense nucleic acid that specifically hybridizes to a target nucleic acid or ribozyme that specifically recognizes the target nucleic acid. The target nucleic acid encodes US28, human UL33 or human UL78. The (A) is a vaccine which generates an immune response in an animal, where the vaccine is attenuated through inhibition of expression or activity of US28 or US28 homolog. The vaccine comprises an immunogenic human **cytomegalovirus** (HCMV) polypeptide encoded by at least a region of hCMV genome in which the polynucleotide segment US28 or UL33 or UL78 has been inactivated. The **CMV** titer is reduced by 5-fold or greater as measured in blood, saliva or urine, following administration of (A). The interference results in a delay in appearance or reduction of levels of reactive leucocyte in the peripheral blood of the animal.
Preferred Sequence: (I) is encoded by a nucleic acid segment that hybridizes under stringent conditions to a sequence comprising 1085, 990, 1019, 991, 1460, 1150, 996 or 1339 nucleotides fully defined in the specification. The immunogenic **CMV** polypeptide in (III) is an HCMV polypeptide encoded by at least a region of the HCMV genome.

ABEX UPTX: 20020618

WIDER DISCLOSURE - Disclosed are pharmaceutical compositions for prophylactically or therapeutically treating **CMV** infections.

SPECIFIC SEQUENCES - (I) comprises a sequence of 344, 339, 340, 328, 485, 401 or 423 amino acids fully defined in the specification, and are encoded by a sequence comprising 1085, 990, 1019, 991, 1460, 1150, 996 or 1339 nucleotides fully defined in the specification (claimed).

ADMINISTRATION - (III) is administered through oral, intranasal, intraperitoneal, intravenous, intramuscular, subcutaneous, subdermal or transdermal route. The dosage is 0.05-20 mg/kg, preferably 1-10 mg/kg/day.
EXAMPLE - Rhesus dermal fibroblasts (RhDF) were infected with rhesus **cytomegalovirus** (**CMV**) strain 68.1. At 96 hours post infection supernatants were collected, and virions were pelleted. The isolated virions were resuspended in TE buffer and proteinase K added to a final concentration of 0.2 microg/ml, sodium dodecyl sulfate to a final concentration of 1% and RnaseA to a final concentration of 10 microg/ml. The resulting mixture was incubated for 2 hours at 65degreesC. Viral DNA was precipitated with ethanol and then subjected to sequencing. The DNA was used to create a shot gun library using hydroshearing and producing inserts of about 3000 nucleotides in length. Individual clones were sequenced using ABI Prism BigDye terminator chemistry. The 220 kb genome was covered to an average accuracy of 6x sequence. Individual reads were assembled into contiguous fragments. Homologs of human **CMV** genes were elucidated using the basic local alignment search tool X program. Sequence was further analyzed using the BioNavigator bio-informatic program set. Analysis of the rhCMV genome indicated the presence of a number of open reading frames having homology with the human **CMV** US28 open reading frame. The regions of homology were referred to as rhUS28.1 (comprising 344 nucleotides), rhUS28.2 (comprising 339 nucleotides), rhUS28.3 (comprising 340 nucleotides), rhUS28.4 (comprising 328 nucleotides) and rhUS28.5 (comprising 485 nucleotides). Other regions having homology to human UL33 and human UL78 were also identified and named rhUL33 (comprising 401 nucleotides), rhUL33 spliced (comprising 365 nucleotides) and rhUL78 (comprising 423 nucleotides) (sequences fully

defined in the specification).

L72 ANSWER 8 OF 8 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN
AN 2002-304220 [34] WPIX
CR 2002-269444 [31]; 2002-351718 [38]
DNC C2002-088487
TI Diagnosis of **cytomegalovirus** useful for treating **cytomegalovirus** infection involves the use of a detectable and a labeled amount of an image generating non-endogenous substituted aromatic compound.
DC B02 B03 B04 D16 K08 S03
IN DAIRAGHI, D J; MCMASTER, B E; **SCHALL, T J**
PA (CHEM-N) **CHEMOCENTRYX INC**; (CHEM-N) **CHEMOCENTRYX**
CYC 97
PI WO 2002017969 A2 20020307 (200234)* EN 28p A61K051-04
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PH PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 2001087007 A 20020313 (200249) A61K051-04
US 2002127544 A1 20020912 (200262) C12Q001-70
US 2002193374 A1 20021219 (200303) A61K051-00
ADT WO 2002017969 A2 WO 2001-US27269 20010830; AU 2001087007 A AU 2001-87007 20010830; US 2002127544 A1 Provisional US 2000-228974P 20000830, Provisional US 2000-229191P 20000830, Provisional US 2000-229365P 20000830, US 2001-944163 20010830; US 2002193374 A1 Provisional US 2000-229191P 20000830, US 2001-944051 20010830
FDT AU 2001087007 A Based on WO 2002017969
PRAI US 2000-229191P 20000830; US 2000-228974P 20000830; US 2000-229365P 20000830; US 2001-944163 20010830; US 2001-944051 20010830
IC ICM A61K051-00; A61K051-04; C12Q001-70
ICS A61K031-40; A61K031-445; A61K031-473; A61K031-495; A61K031-498; A61K031-519; A61K031-535
AB WO 200217969 A UPAB: 20030113
NOVELTY - Diagnosis of **cytomegalovirus** (**CMV**) involves administering an image-generating compound to a subject having **CMV**.

DETAILED DESCRIPTION - Diagnosis of **cytomegalovirus** (**CMV**) involves administering an image generating compound of formula Ar-C(=O)-N(R11)-CH2-A (I) or its salt.

Ar = substituted aryl group;

R11 = H or optionally substituted 1-4C alkyl; and

A = optionally substituted 4-7 membered nitrogen heterocycle.

INDEPENDENT CLAIMS are also included for the followings:

(1) treating **CMV** in a human involving administering a compound, which blocks the binding of a chemokine to US28 or its fragment; and

(2) reducing cell motility in a **CMV**-infected cell involving contacting the cell with a motility-reducing compound that inhibits chemokine binding to US28 on the surface of the cell.

ACTIVITY - Virucide.

MECHANISM OF ACTION - Blocker and inhibitor of chemokine (preferably fractalkine, MIP-1 alpha , MIP-1 beta , MCP-1 or RANTES) binding.

US28 expressing cells consisted of a mouse cell line stably expressing transfected US28 cDNA under the control of **CMV** promoter were cultured in IMDM-5% FBS and harvested at the concentration of 0.5 - 1 multiply 106 cells/ml. The cells were centrifuged and resuspended in assay buffer (HEPES (20 mM), sodium chloride (140 mM), calcium chloride (1 mM), magnesium chloride (5 mM) and with bovine serum albumin (0.2%)) to a concentration of 5.6 multiply 106 cells/ml. First cells (0.09 ml) was added to 8 assay plates containing

S-(-)-3-iodo-2-hydroxy-6-methoxy-N((1-ethyl-2-pyrrolidinyl)methyl)-benzamide (a) (having a final concentration of 5 micro g/ml). 125I-Fractalkine (0.09 ml) diluted in assay buffer was added, the plates sealed and incubated for 3 hours at 4 deg. C. The assay plates were harvested, pre-soaked in PEI solution. Scintillation fluid (35 micro l) was added to all wells, the plates were sealed and counted. Control wells containing diluent or excess fractalkine were used to calculate % of total inhibition for (a). The IC50 of (a) against fractalkine binding on US28-NSO cell was 0.6 micro M.

USE - For diagnosis of **CMV**, for treating **CMV** in a human and for reducing cell motility in a **CMV**-infected cell (claimed); in PET (undefined), SPET (undefined) and tracer analysis.

ADVANTAGE - The compound inhibits chemokine binding to US28 on the surface of a **CMV**-infected cell or blocks the chemokine binding to US28 or its fragment. The compound provides IC50 value of at most 50 (preferably at most 20, more preferably at most 10, especially less than 1) micro g/ml.

Dwg.0/3

FS CPI EPI

FA AB; GI; DCN

MC CPI: B07-D03; B07-H; B14-A02; B14-L06; K08-X; K09-E

TECH UPTX: 20020528

TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preferred Compound: The compound is labeled with a radioisotope selected from 18F, 75Br, 123I or 125I.

ABEX UPTX: 20020528

SPECIFIC COMPOUNDS - 3-Iodo-2-hydroxy-6-methoxy-N((1-ethyl-2-pyrrolidinyl)methyl)-benzamide (IBZM) and 123I-IBZM are specifically claimed as (I).

ADMINISTRATION - The compound can be administered orally, topically, rectally or parenterally (including intramuscularly, intravenously or subcutaneously) in a dosage of about 2-2000 mg per day. For oral route, the dosage of (I) is 0.05-20 (preferably 0.05-2, especially 0.05-0.2) mg/kg of body weight per day, and for parenteral administration is 0.01-250 (preferably 1-10, more preferably 0.5-30, especially 1-20) mg/kg/day.

EXAMPLE - No relevant example given.

DEFINITIONS - Preferred Definitions:
Ar = substituted phenyl;
A = pyrrolidinyl, piperazinyl, piperidinyl, morpholinyl or piperidyl (all optionally substituted);
R11 = H;
R12 - R14 = H, -OH, halo, 1-4C alkyl or 1-4C alkoxy;
R15 = 1-4C alkyl.
Preferably (I) is a compound of formula (Ia).
n = 1-3 (preferably 1);
R15 = R11;
R12 - R14 = H, OH, halo, 1-4C (halo)alkyl, 1-4C (halo)alkoxy, nitro, cyano, 1-4C acyl, (1-4C alkyl)amino or di(1-4C)alkylamino.
With the proviso that at least one of R12 - R14 is other than H and that (i) when n is 1, R11 is H, R12 - R14 are H, OH, halo, 1-4C alkyl or 1-4C alkoxy and R15 is 1-4C alkyl or when n is 1, R11 is H, R15 is 1-4C alkyl then R12 - R14 are all other than H.

=> => d his

(FILE 'HOME' ENTERED AT 08:04:17 ON 30 JAN 2004)
DEL HIS

FILE 'REGISTRY' ENTERED AT 08:05:18 ON 30 JAN 2004

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L1              STR
L2           50 S L1
L3         1769 S L1 FUL
                SAV TEMP L3 LE061/A
L4              STR L1
L5           25 S L4 CSS SAM SUB=L3
L6          561 S L4 CSS FUL SUB=L3
                SAV TEMP L6 LE061A/A
L7              STR L4
L8           19 S L7 CSS SAM SUB=L6
L9          457 S L7 CSS FUL SUB=L6
                SAV TEMP L9 LE061B/A

     FILE 'HCAPLUS' ENTERED AT 08:20:19 ON 30 JAN 2004
L10          618 S L9
L11        13257 S CMV OR ?CYTOMEGALOVIR?
                E CYTOMEGALOVIR/CT
                E E4+ALL
L12         2971 S E7
L13         5744 S E6+NT
                E CYTOMEG/CT
                E E6+ALL
L14            2 S L10 AND L11-L13
                E SCHALL T/AU
L15          128 S E3-E10
                E PENFOLD M/AU
L16           17 S E4-E6
                E CHEMOCENTR/PA,CS
L17           33 S E5-E14
                E CHEMO CENTR/PA,CS
L18            2 S L10 AND L15-L17
L19            1 S US20020182594/PN OR (WO2002-US3229 OR US2001-266094#)/AP,PRN
L20            3 S L14,L18,L19
L21            3 S L20 AND L10-L20
                SEL HIT RN

     FILE 'REGISTRY' ENTERED AT 08:24:11 ON 30 JAN 2004
L22            4 S E1-E4

     FILE 'REGISTRY' ENTERED AT 08:24:33 ON 30 JAN 2004

     FILE 'MEDLINE' ENTERED AT 08:24:56 ON 30 JAN 2004
L23          356 S L9
L24          989 S OCTOCLOTHEPIN? OR CLOTEPIN? OR CLOTHEPIN? OR CLOROTHEPIN? OR
L25          989 S L23,L24
L26        28347 S L11
                E CYTOMEGALOVIR/CT
                E E6+ALL
L27        11117 S E9+NT
                E CYTOMEGALOVIR/CT
                E E9+ALL
L28        14342 S E5+NT
                E CYTOMEGALOVIR/CT
                E E77+ALL
L29           22 S E10+NT
                E CYTOMEGALOVIRUS/CT
                E E82+ALL
L30         1546 S E2+NT
L31          351 S E4+NT
L32            0 S L25 AND L26-L31
                E SCHALL T/AU
L33           89 S E3-E7
                E PENFOLD M/AU
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L34          12 S E3-E5,E8,E9
L35           0 S L25 AND L33,L34
L36          10 S L26-L31 AND L33,L34

     FILE 'BIOSIS' ENTERED AT 08:31:11 ON 30 JAN 2004
L37        1228 S L25
L38       31590 S L11
L39       82214 S HERPESVIRIDAE+NT/BC
                E 02220/BC
                E 02162/BC
                E CYTOMEGA/BC
                E HERP/BC
L40           0 S L37 AND L38,L39
                E SCHALL T/AU
L41         146 S E3-E9
                E PENFOLD M/AU
L42          13 S E4-E7
L43           0 S L37 AND L41,L42
L44          16 S L38,L39 AND L41,L42

     FILE 'MEDLINE, BIOSIS' ENTERED AT 08:49:21 ON 30 JAN 2004
L45          16 DUP REM L36 L44 (10 DUPLICATES REMOVED)

     FILE 'REGISTRY' ENTERED AT 08:49:32 ON 30 JAN 2004

     FILE 'HCAPLUS' ENTERED AT 08:49:55 ON 30 JAN 2004

     FILE 'MEDLINE, BIOSIS' ENTERED AT 08:50:44 ON 30 JAN 2004

     FILE 'WPIX' ENTERED AT 08:51:22 ON 30 JAN 2004
L46        3651 S L11/BIX
L47          61 S C07K014-045/IC,ICM,ICS,ICA,ICI
L48         328 S C12N015-38/IC,ICM,ICS,ICA,ICI
L49        1927 S (B04-B02B4 OR C04-B02B4)/MC
L50        5359 S (B04-F11 OR C04-F11)/MC
L51        6234 S (D05-H06 OR D05-H06A OR D05-H12F)/MC
L52          93 S (D430(S)F553)/M0,M1,M2,M3,M4,M5,M6
L53          20 S L24/BIX
                E OCTOCLOTHEPIN/DCN
                E CLOTEPIN/DCN
                E METITEPIN/DCN
                E METHIOTEPIN/DCN
L54           0 S L46-L51 AND L52
L55           1 S L46-L51 AND L53
                E SCHALL T/AU
L56          29 S E3-E5
                E PENFOLD M/AU
L57          10 S E3,E4
                E CHEMOCENT/PA
L58          24 S E4,E5
L59          10 S L46-L51 AND L56-L58
L60           1 S L52,L53 AND L56-L58
L61          10 S L55,L59,L60
L62           1 S L19
L63          10 S L62,L61 AND L46-L62
L64           1 S L55 AND L63
L65           9 S L63 NOT L64
L66         325 S (D420(S)F553)/M0,M1,M2,M3,M4,M5,M6
L67           3 S L66 AND L46-L51
L68          11 S L67,L63-L65
L69           1 S L68 NOT L63
L70          10 S L68 NOT L69
L71           2 S L70 AND L67
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L72           8 S L70 NOT L71

     FILE 'WPIX' ENTERED AT 09:09:04 ON 30 JAN 2004
L73       13897 S L46-L51
L74        1899 S L73 AND C12Q001-70/IC,ICM,ICS
L75        3256 S L73 AND G01N033-5?/IC,ICM,ICS
L76        6527 S L73 AND (B12-K04? OR C12-K04?)/MC
L77          90 S (B06-B02 OR C06-B02)/MC AND (B07-D05 OR C07-D05)/MC
L78         465 S L77,L52,L53,L66
L79           3 S L78 AND L73
L80           1 S L79 NOT L70
L81           1 S L80,L69

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